REMARKS

Preliminary Remarks

Claims 107-111 and 117-132 are currently pending and are under examination. Claims 1-88, 89, and 102-106 were previously canceled. Applicants respectfully request entry of the remarks made herein into the file history of the present application.

Patentability Arguments

A. The Rejections of Claims 107-111 and 117-132 Under 35 U.S.C. §§ 103(a) Should Be Withdrawn

Claims 107-111 and 117-132 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Bram *et al.* (WO 98/39361) (hereinafter "Bram PCT") in view of Presta et al. (U.S. Patent No. 5,739,277) (hereinafter "Presta") for "reasons of record."

Claims 107-111 and 117-132 also stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Bram *et al.* (US Patent No. 5,969,102) (hereinafter "Bram US") in view of Presta et al. (U.S. Patent No. 5,739,277) (hereinafter "Presta") for "reasons of record."

Applicants respectfully traverse these rejections in view of the following arguments.

i. The Legal Standard for Obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the Examiner must provide a clear articulation of the reasons why the claimed invention would have been obvious, i.e., the Examiner must provide a reason one of ordinary skill in the art would have combined the cited references to arrive at the claimed invention. Second, there must be a reasonable expectation of success. That is, the hypothetical person of ordinary skill in the art, at the time the invention was made, must have had a reasonable expectation that the proposed modification or combination would work to produce beneficial results. *See* MPEP § 2143.02. Finally, "to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981 (CCPA 1974). The burden of establishing a *prima facie* case of obviousness lies with the Examiner, and the expectation of success must be found in the prior art, not the applicant's disclosure. *In re Dow Chemical*, 5 USPQ 2d 1531 (Fed. Cir. 1988).

Where the claims at issue are directed to molecules having a specific structure and the prior art provides a vast genus of molecules including those claimed but fails to suggest the claimed molecules, the Federal Circuit has repeatedly held that such claims are nonobvious.

In *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993) the claims at issue were drawn to specific nucleotide sequences representing cDNAs encoding human IGF I and II. The U.S. Patent and Trademark Office Board of Patent Appeals and Interferences held the claims unpatentable as obvious in view of prior art references disclosing (1) the complete amino acid sequence of each protein and (2) a general cloning method. In reversing the Board, the Federal Circuit noted that of the vast number of nucleotide sequences encoding IGF I and II, Bell was claiming only 2: the human cDNA sequences set forth in the application. The Court found that regardless of how obvious it might have been to use the prior art cloning method, the issue is the obviousness of the compositions claimed not the method by which they were obtained. Since nothing in the cited prior art references indicated which of the vast number of hypothetical coding sequences would turn out to be actual IGF I and II cDNA sequences, the Court found the narrowly claimed invention non-obvious: "the failure of the cited prior art to suggest which of those possibilities is the human sequence [means that] the claimed sequences would not have been obvious" (emphasis added)." *Id.* at 784. *See also In re Thorpe*, 777 F.2d 695, 697, 227 USPQ 964, 966 (Fed. Cir. 1985) ("The patentability of a product does not depend on its method of production.").

In *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995), the Court again overturned a decision of the Board rejecting claims to specific nucleic acid molecules (here encoding heparin-binding growth factors (HBGFs) for obviousness in view of prior art references describing: (1) partial polypeptide sequence of HBGF and (2) a method for isolating DNA/cDNA given partial protein sequence. According to the Court:

> A prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein. No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate it should be prepared (emphasis added). *Id.* at 1558-1559.

Moreover, the Court found that the Board had improperly rejected the claims based on the alleged obviousness of a method of making the molecules:

> We today reaffirm the principle, stated in Bell, that the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs…A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out (emphasis added). *Id.* at 1559.

Recently, the U.S. Supreme Court in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007), found that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of **identified, predictable solutions**, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." (emphasis added). *Id.* at 1732. Thus, in certain limited situations, a *prima facie* case of obviousness may be predicated on an 'obvious to try' analysis. However, such an analysis is not proper unless: (1) the art is predictable and (2) the solutions are identified, small in number and easily traversed in the context of the art. *See, e.g. Ortho-McNeil Pharmaceutical v. Mylan Labs*, 520 F.3d 1358 (Fed. Cir. 2008) (holding that the cited passage of *KSR* is applicable only in the case of an "easily traversed, small and finite number of alternatives" and is not properly applied if the alternatives are "unpredictable") (emphasis added).

ii. Analysis

Applicants respectfully submit that the cited references, alone or in combination, fail to teach or suggest all the claim limitations. Moreover, Applicants respectfully submit that the Examiner applied an improper standard in finding the pending claims obvious. For at least these reasons, the Examiner has failed to establish a *prima facie* case of obviousness.

The Examiner acknowledges, at pages 6 and 10 of the Final Office Action, that Bram PCT and Bram US each fails to disclose TACI extracellular sub-fragments consisting of amino acid residues 25-104 or 1-154 of SEQ ID NO: 6. However, according to the Examiner, it would have been obvious to the skilled artisan to produce the specifically claimed fragments of the extracellular domain and test them for observed biological activity. In other words, the Examiner bases his finding of obviousness on the availability of techniques by which the specifically claimed fragments might have been obtained. However, binding Federal Circuit

case law, which has not been overturned, provides that "a general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." Here, the specifically claimed fusion proteins comprising a first portion consisting of the claimed TACI fragments are simply not disclosed by Bram PCT or Bram US nor is any guidance provided therein through which one of ordinary skill in the art might obtain such specific fusion proteins. The Examiner is not free to disregard such precedent.

Moreover, the Examiner's reliance on *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007) is misplaced. *KSR* did not overrule *In re Bell* or *In re Deuel* and regardless, is inapplicable on its own terms. In order to properly apply an "obvious to try" standard, (1) the art must be predictable and (2) the solutions must be identified, small in number and easily traversed in the context of the art. *See, e.g. Ortho-McNeil Pharmaceutical v. Mylan Labs*, 520 F.3d 1358 (Fed. Cir. 2008). Neither condition is met in the instant case. First, biological and chemical processes are unpredictable; as discussed below, the instant invention derives from an unpredictable result and therefore is not obvious. This unpredictability has been explicitly acknowledged by the Examiner in prior Office communications. *See, e.g.*, Office communication mailed May 23, 2005 at page 22 (stating that "the art is unpredictable"). Second, the prior art did not present a small and easily traversed number of options to the skilled artisan. Rather, as previously discussed, the prior art disclosed only that the ligand binding portion of TACI lies somewhere within the extracellular domain.

In their previous response, Applicants provided evidence that at the time of the instant invention it was not predictable that the specifically claimed TACI fragments would bind BLyS removed from the context of the full-length polypeptide. These references are now listed on an Information Disclosure Statement, submitted herewith. The references demonstrate that the transmembrane domain of a variety of cell receptor proteins contribute to ligand binding in these proteins.[1] Moreover, the references demonstrate that amino acids immediately adjacent to the transmembrane domain have been shown to play a crucial role in the proper folding of the

[1] Lin, J.C. *et al.*, Mol. Cell. Biol. 24(5):2041-2051 (reference A33) (2004) ("residues at the extracellular ends of transmembrane domains of G protein-coupled receptors have been found to contribute to ligand binding"); Liapakis, G. *et al.*, J. Biol. Chem. 271(34):20331-20339 (1996) (reference A34) (describing a transmembrane region of somatostatin receptors 1 and 2 essential for ligand-binding)

extracellular domains of, and the ligand binding capacity of, several signal transducing proteins.[2] Thus, one of ordinary skill in the art would comprehend the inherent unpredictability with regard to the ability of the specifically disclosed and claimed fusion proteins to retain ligand binding capability as required by the instantly pending claims. Such unpredictability precludes application of an "obvious to try" analysis to arrive at the missing claim limitations.

Moreover, while there may exist a finite number of fragments of the extracellular domain, the Examiner fails to appreciate the scope of possible fragments which extends at least into the thousands, precluding contemplation of or focus on the specifically claimed TACI fragments. Not a single such fragment is identified by Bram PCT or Bram US. In fact, Bram PCT and Bram US each only makes a general statement that the ligand binding domain is located somewhere within the TACI extracellular domain. Neither reference discloses the currently claimed fragments, nor does either reference identify a TACI ligand which could be used to identify which, if any, of the thousands of extracellular fragments retain ligand binding capability. Thus, there is simply no way to predict from Bram PCT or Bram US that the currently claimed fragments would constitute ligand-binding fragments. The claimed fusion proteins cannot be obvious where the prior art does not lead the skilled artisan to the specifically claimed fragments especially given there is no ligand identified which could be used to identify such ligand binding fragments. In this regard, the facts of the instant case closely track those present in the binding Federal Circuit cases of *In re Bell* and *In re Deuel*, discussed *supra*.

The Examiner comments on page 8 of the Final Office Action that "it is unclear how Applicant determined that there were 'thousands' of possible fragments given that the extracellular domain of TACI (SEQ ID NO:6) is 166 amino acids in length." For a polypeptide of a given length, there is an inverse relationship between the number of potential fragments that can be constructed and the size of a given fragment. For a polypeptide of 166 amino acids (corresponding to the TACI extracellular domain), there are 157 ten-amino acid fragments, 156

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[2] Leiter, E.H. & Lee, C-H., Diabetes 54 (Suppl. 2):S151-S158 (2005) (reference A35) (G-to-T transversion at portion of extracellular domain immediately adjacent to transmembrane domain thought to affect nearby ligand binding domain of leptin receptor and reduce signaling through the receptor); Excoffon, K. *et al.*, Am. J. Respir. Cell. Mol. Biol. 32:498-503 (2005) (reference A36) (intact Coxsackievirus B and Adenovirus Receptor extracellular domain required for efficient ligand binding and infection)(emphasis added); Wada A., *et al.*, Infect. Immun. 64(12):5144-5150 (1996) (reference A37) ("the region adjacent to the [guanylyl cyclase] transmembrane domain plays an important role in facilitating a favorable conformation…for heat stable enterotoxin binding.")

eleven-amino acid fragments, 155 twelve-amino acid fragments and so forth. Excluding fragments below 10 amino acids, there are total of (157 + 156 + 155....+ 3 + 2) or 12,402 fragments. One of the claimed fragments consists of amino acid residues 25-104, corresponding to an 80 amino acid fragment. For the TACI extracellular domain, there are 87 possible 80-amino acid fragments. In any event, the genus of potential fragments is vast and the prior art provides no guidance which could lead the skilled artisan to those specifically claimed.

With respect to the Examiner's statements on pages 8-9 of the Final Office Action that "techniques for determining binding domains of a given ligand or receptor is part of the ordinary capabilities of a person of ordinary skill in the art," the Examiner has failed to support such statements with evidence of how such binding domains could be determined in the absence of a ligand without recourse to inventive work. At any rate, the pending claims recite the use of specific TACI fragments, not ligand binding portions generally.

The disclosure of Presta does nothing to rectify the aforementioned failure of Bram PCT and Bram US to disclose the specifically claimed fragments.

Based on the aforementioned, it is clear that the Examiner has improperly applied an "obvious to try" standard in finding the claims obvious over the cited prior art. Here, the prior art teaches generally that the ligand binding portion of TACI is located somewhere on the extracellular domain. While it might have been obvious to make and screen the multitude of fragments representing all possible overlapping peptides derived from the protein in order to find a ligand binding fragment, the prior art does nothing to direct one of ordinary skill toward any particular fragment and certainly not toward the claimed fragment. *See, e.g. In re Duel*, 51 F.3d 1552, 1559 (Fed Cir 1995) ("There must, however, still be prior art that suggest the claimed compound in order for prima facie case to be made out."). Thus, the pending claims are, as a matter of law, nonobvious over each of Bram PCT and Bram US in view Presta under 35 U.S.C. § 103(a) and the Applicants respectfully request withdrawal of the rejections.

B. <u>The Rejections for Obviousness-type Double Patenting</u>

Claims 107-109, 117-119 and 122-123 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 of copending Application No. 11/748,978. Applicants wish to defer the response to these provisional rejections until the claims are otherwise allowable.

Conclusion

In view of the above remarks, applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at (312) 595-1408. Should any additional fees be deemed necessary in connection with the filing of this document, the Commissioner is hereby authorized to deduct any such fees from Deposit Account No. 08-3038 referencing the above attorney docket number.

Respectfully submitted,

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991 F.2d 781
991 F.2d 781, 61 USLW 2692, 26 U.S.P.Q.2d 1529

▷

United States Court of Appeals,Federal Circuit.
In re Graeme I. BELL, Leslie B. Rall and James P. Merryweather.
No. 92-1375.

April 20, 1993.

Patent applicants sought appeal following examiner's final rejection of various claims as unpatentable on ground of obviousness. The Patent and Trademark Office Board of Patent Appeals affirmed, and applicants appealed. The Court of Appeals, Lourie, Circuit Judge, held that claims of patent application directed to nucleic acid molecules containing human sequences which code for human insulin-like growth factors I and II were not unpatentable on ground of obviousness.

Reversed.

West Headnotes

[1] Patents 291 ⚿16.14

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.14 k. Miscellaneous Inventions. Most Cited Cases
Claims of patent application directed to nucleic acid molecules containing human sequences which code for human insulin-like growth factors I and II, single chain serum proteins that play role in mediation of somatic cell growth following administration of growth hormones, were not unpatentable on ground of obviousness; amino acid sequence of protein in conjunction with reference indicating general method of cloning did not render gene prima facie obvious. 35 U.S.C.A. § 103.

[2] Patents 291 ⚿114.16

291 Patents
291IV Applications and Proceedings Thereon
291k114.15 Hearing and Scope of Inquiry
291k114.16 k. In General; Trial De Novo. Most Cited Cases
Court of Appeals reviews obviousness determination by Patent and Trademark Office Board of Patent Appeals de novo.

[3] Patents 291 ⚿114.19

291 Patents
291IV Applications and Proceedings Thereon
291k114.15 Hearing and Scope of Inquiry
291k114.19 k. Presumptions and Burden of Proof. Most Cited Cases
Patent and Trademark Office bears burden of establishing case of prima facie obviousness.

[4] Patents 291 ⚿16(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16 Invention and Obviousness in General
291k16(1) k. In General. Most Cited Cases
For purpose of determining whether claimed patent is prima facie obvious, what reference teaches and whether it teaches toward or away from claimed invention are questions of fact.

***782** Robert P. Blackburn, Chiron Corp., Emeryville, CA, argued for appellant. With him on the brief were Debra A. Shetka and Thomas E. Ciotti, Morrison & Foerster, Palo Alto, CA, and Donald S. Chisum, Morrison & Foerster, Seattle, WA.
Teddy S. Gron, Associate Sol., Office of the Sol., Arlington, VA, argued for appellee. With him on the brief was Fred E. McKelvey, Sol. Of counsel were John W. Dewhirst, Lee E. Barrett, Richard E. Schafer and Albin F. Drost.

Before RICH, LOURIE, and SCHALL, Circuit Judges.

LOURIE, Circuit Judge.

Applicants Graeme I. Bell, Leslie B. Rall, and James P. Merryweather (Bell) appeal from the March 10, 1992 decision of the U.S. Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences, Appeal No. 91-1124, affirming the examiner's final rejection of claims 25-46 of application Serial No. 065,673, entitled "Preproinsulin-Like Growth Factors I and II," as unpatentable on the ground of obviousness under 35 U.S.C. § 103 (1988). Because the Board erred in concluding that the claimed nucleic acid molecules would have been obvious in light of the cited prior art, we reverse.

BACKGROUND

The claims of the application at issue are directed to nucleic acid molecules (DNA and RNA) [FN1] containing human sequences [FN2] which code for human insulin-like growth factors I and II(IGF), single chain serum proteins that play a role in the mediation of somatic cell growth following the administration of growth hormones.[FN3]

FN1. A basic familiarity with recombinant DNA technology is presumed. For a general discussion, *see In re O'Farrell,* 853 F.2d 894, 895-99, 7 USPQ2d 1673, 1674-77 (Fed.Cir.1988).

FN2. Interchangeably referred to as "native" sequences and "genes."

FN3. Claim 25 is conceded to be representative of the claims at issue:

> A composition comprising nucleic acid molecules containing a human sequence encoding insulin-like growth factor (hIGF) substantially free of nucleic acid molecules not containing said hIGF sequence, wherein said hIGF sequence is selected from the group consisting of:
>
> (a) 5'-GGA CCG GAG ACG CUC UGC GGG GCU GAG CUG GUG GAU GCU CUU CAG UUC GUG UGU GGA GAC AGG GGC UUU UAU UUC AAC AAG CCC ACA GGG UAU GGC UCC AGC AGU CGG AGG GCG CCU CAG ACA GGU AUC GUG GAU GAG UGC UGC UUC CGG AGC UGU GAU CUA AGG AGG CUG GAG AUG UAU UGC GCA CCC CUC AAG CCU GCC AAG UCA GCU-3', wherein U can also be T;
>
> (b) 5'-GCU UAC CGC CCC AGU GAG ACC CUG UGC GGC GGG GAG CUG GUG GAC ACC CUC CAG UUC GUC UGU GGG GAC CGC GGC UUC UAC UUC AGC AGG CCC GCA AGC CGU GUG AGC CGU CGC AGC CGU GGC AUC GUU GAG GAG UGC UGU UUC CGC AGC UGU GAC CUG GCC CUC CUG GAG ACG UAC UGU GCU ACC CCC GCC AAG UCC GAG-3', wherein U can also be T;
>
> (c) nucleic acid sequences complementary to (a) or (b); and
>
> (d) fragments of (a), (b) or (c) that are at least 18 bases in length and which will selectively hybridize to human genomic DNA encoding hIGF.
>
> The other rejected claims are apparently directed to cellular hosts transformed with the claimed nucleic acid sequences. Because their fate is dependent upon that of claim 25, neither appellant nor the Patent and Trademark Office have considered them separately and we will not do so either.

***783** The relevant prior art consists of two publications by Rinderknecht [FN4] disclosing amino acid sequences for IGF-I and -II and U.S. Patent 4,394,443 to Weissman et al., entitled "Method for Cloning Genes." Weissman describes a general method for isolating a gene for which at least a

short amino acid sequence of the encoded protein is known. The method involves preparing a nucleotide probe corresponding to the known amino acid sequence and using that probe to isolate the gene of interest. It teaches that it is advantageous to design a probe based on amino acids specified by unique codons.[FN5] The Weissman patent specifically describes the isolation of a gene which codes for human histocompatibility antigen, a protein unrelated to IGF. It describes the design of the probe employed, stating that it was based on amino acids specified by unique codons.

> FN4. Rinderknecht et al., *The Amino Acid Sequence of Human Insulin-like Growth Factor I and Its Structural Homology with Proinsulin,* 253 The Journal of Biological Chemistry 2769-76 (1978); Rinderknecht et al., *Primary Structure of Human Insulin-like Growth Factor II,* 89 FEB Letters 283-86 (May 1978).

> FN5. A sequence of three nucleotides, called a codon, codes for each of the twenty natural amino acids. Since there are twenty amino acids and sixty-four possible codons, most amino acids are specified by more than one codon. This is referred to as "degeneracy" in the genetic code. The term "unique" refers to an amino acid coded for by a single codon. *See Amgen Inc. v. Chugai Pharmaceutical Co.,* 927 F.2d 1200, 1207-08 n. 4, 18 USPQ2d 1016, 1022 n. 4 (Fed.Cir.), *cert. denied,* 502 U.S. 856, 112 S.Ct. 169, 116 L.Ed.2d 132 (1991).

The examiner rejected the claims as obvious over the combined teachings of Rinderknecht and Weissman. She determined that it would have been obvious, "albeit tedious," from the teachings of Weissman to prepare probes based on the Rinderknecht amino acid sequences to obtain the claimed nucleic acid molecules. According to the examiner, "it is clear from [Weissman] that the ordinary artisan knows how to find the nucleic acid when the amino acid sequence is known" and that "the claimed sequences and hosts would have been readily determinable by and obvious to those of ordinary skill in the art at the time the invention was made."

The Board affirmed the examiner's rejection, holding that the examiner had established a *prima facie* case of obviousness for the claimed sequences "despite the lack of conventional indicia of obviousness, e.g., structural similarity between the DNA which codes for IGF-I and the amino acid sequence of the polypeptide which constitues [sic] IGF-I." Slip op. at 6. The Board reasoned that "although a protein and its DNA are not structurally similar, they are correspondently linked via the genetic code." *Id.* at 4 n. 1. In view of Weissman, the Board concluded that there was no evidence "that one skilled in the art, knowing the amino acid sequences of the desired proteins, would not have been able to predictably clone the desired DNA sequences without undue experimentation." *Id.* at 8.

The issue before us is whether the Board correctly determined that the amino acid sequence of a protein in conjunction with a reference indicating a general method of cloning renders the gene *prima facie* obvious.

DISCUSSION

[1][2] We review an obviousness determination by the Board *de novo. In re Vaeck,* 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed.Cir.1991). Bell argues that the PTO has not shown how the prior art references, either alone or in combination, teach or suggest the claimed invention, and thus that it has failed to establish a *prima facie* case of obviousness.

[3] We agree. The PTO bears the burden of establishing a case of *prima facie* obviousness. *In re Fine,* 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed.Cir.1988). "A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed

subject matter to a person of ordinary skill in the art." *In re Rinehart,* 531 F.2d 1048, 1051, 189 USPQ 143, 147 (CCPA 1976).

The Board supported the examiner's view that the "correspondent link" between ***784** a gene and its encoded protein via the genetic code renders the gene obvious when the amino acid sequence is known. In effect, this amounts to a rejection based on the Rinderknecht references alone. Implicit in that conclusion is the proposition that, just as closely related homologs, analogs, and isomers in chemistry may create a *prima facie* case, *see In re Dillon,* 919 F.2d 688, 696, 16 USPQ2d 1897, 1904 (Fed.Cir.1990) (*in banc*), *cert. denied,* 500 U.S. 904, 111 S.Ct. 1682, 114 L.Ed.2d 77 (1991), the established relationship in the genetic code between a nucleic acid and the protein it encodes also makes a gene *prima facie* obvious over its correspondent protein.

We do not accept this proposition. It may be true that, knowing the structure of the protein, one can use the genetic code to hypothesize possible structures for the corresponding gene and that one thus has the potential for obtaining that gene. However, because of the degeneracy of the genetic code, there are a vast number of nucleotide sequences that might code for a specific protein. In the case of IGF, Bell has argued without contradiction that the Rinderknecht amino acid sequences could be coded for by more than 10^{36} different nucleotide sequences, only a few of which are the human sequences that Bell now claims. Therefore, given the nearly infinite number of possibilities suggested by the prior art, and the failure of the cited prior art to suggest which of those possibilities is the human sequence, the claimed sequences would not have been obvious.

Bell does not claim all of the 10^{36} nucleic acids that might potentially code for IGF. Neither does Bell claim all nucleic acids coding for a protein having the biological activity of IGF. Rather, Bell claims only the human nucleic acid sequences coding for IGF. Absent anything in the cited prior art suggesting which of the 10^{36} possible sequences suggested by Rinderknecht corresponds to the IGF gene, the PTO has not met its burden of establishing that the prior art would have suggested the claimed sequences.

This is not to say that a gene is never rendered obvious when the amino acid sequence of its coded protein is known. Bell concedes that in a case in which a known amino acid sequence is specified exclusively by unique codons, the gene might have been obvious. Such a case is not before us.[FN6] Here, where Rinderknecht suggests a vast number of possible nucleic acid sequences, we conclude that the claimed human sequences would not have been obvious.

> FN6. We also express no opinion concerning the reverse proposition, that knowledge of the structure of a DNA, e.g., a cDNA, might make a coded protein obvious.

[4] Combining Rinderknecht with Weissman does not fill the gap. Obviousness " 'cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination.' " *In re Fine,* 837 F.2d at 1075, 5 USPQ2d at 1598 (citing *ACS Hosp. Sys. v. Montefiore Hosp.,* 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed.Cir.1984)). What a reference teaches and whether it teaches toward or away from the claimed invention are questions of fact. *See Raytheon Co. v. Roper Corp.,* 724 F.2d 951, 960-61, 220 USPQ 592, 599-600 (Fed.Cir.1983), *cert. denied,* 469 U.S. 835, 105 S.Ct. 127, 83 L.Ed.2d 69 (1984).

While Weissman discloses a general method for isolating genes, he appears to teach away from the claimed invention by emphasizing the importance of unique codons for the amino acids. Weissman suggests that it is generally advantageous to design a probe based on an amino acid sequence specified by unique codons, and also teaches that it is "counterproductive" to use a primer having more than 14-16 nucleotides unless the known amino

acid sequence has 4-5 amino acids coded for by unique codons. Bell, in contrast, used a probe having 23 nucleotides based on a sequence of eight amino acids, none of which were unique. Weissman therefore tends to teach away from the claimed sequences since Rinderknecht shows that IGF-I has only a single amino acid with a unique codon and IGF-II has none.

***785** The PTO, in urging us to affirm the Board, points to the suggestion in Weissman that the disclosed method can "easily" be applied to isolate genes for an array of proteins including peptide hormones. The PTO thus argues that in view of Weissman, a gene is rendered obvious once the amino acid sequence of its translated protein is known. We decline to afford that broad a scope to the teachings of Weissman. While "a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests," *In re Burckel,* 592 F.2d 1175, 1179, 201 USPQ 67, 70 (CCPA 1979), we cannot say that Weissman "fairly suggests" that its teachings should be combined with those of Rinderknecht, since it nowhere suggests how to apply its teachings to amino acid sequences without unique codons.

We conclude that the Board clearly erred in determining that Weissman teaches toward, rather than away from, the claimed sequences. Therefore, the requisite teaching or suggestion to combine the teachings of the cited prior art references is absent, *see In re Fine,* 837 F.2d at 1075, 5 USPQ2d at 1599, and the PTO has not established that the claimed sequences would have been obvious over the combination of Rinderknecht and Weissman.

Finally, the PTO emphasizes the similarities between the method by which Bell made the claimed sequences and the method taught by Weissman. The PTO's focus on Bell's method is misplaced. Bell does not claim a method. Bell claims compositions, and the issue is the obviousness of the claimed compositions, not of the method by which they are made. *See In re Thorpe,* 777 F.2d 695, 697, 227 USPQ 964, 966 (Fed.Cir.1985) ("The patentability of a product does not depend on its method of production.").

CONCLUSION

Because we conclude that the combination of prior art references does not render the claimed invention obvious, we reverse the Board's decision affirming the examiner's rejection of claims 25-46.

REVERSED.

C.A.Fed.,1993.
In re Bell
991 F.2d 781, 61 USLW 2692, 26 U.S.P.Q.2d 1529

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51 F.3d 1552
51 F.3d 1552, 63 USLW 2624, 34 U.S.P.Q.2d 1210

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United States Court of Appeals,Federal Circuit.
In re Thomas F. DEUEL, Yue-Sheng Li, Ned R. Siegel and Peter G. Milner.
No. 94-1202.

March 28, 1995.

Inventors applied for patent for deoxyribonucleic acid (DNA) and complementary DNA (cDNA) molecules encoding proteins that stimulated cell division. After patent examiner rejected claims as unpatentable on grounds of obviousness and the Patent and Trademark Office Board of Patent Appeals and Interferences affirmed, inventors appealed. The Court of Appeals, Lourie, Circuit Judge, held that: (1) combination of prior art reference teaching method of gene cloning, together with reference disclosing partial amino acid sequence for a protein that stimulated cell division, did not render claims prima facie obvious; (2) conceived method of preparing some unidentified DNA does not define it with precision necessary to render it obvious over protein it encodes; and (3) patent claims generically encompassing all DNA sequences encoding human and bovine proteins to stimulate cell division were not invalid as obvious.

Reversed.

West Headnotes

[1] Patents 291 ⚿314(5)

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k314 Hearing
291k314(5) k. Questions of Law or Fact. Most Cited Cases

Patents 291 ⚿324.55(1)

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k324 Appeal
291k324.55 Questions of Fact, Verdicts, and Findings
291k324.55(1) k. In General. Most Cited Cases
Obviousness is question of law, which Court of Appeals reviews de novo, though factual findings underlying obviousness determination are reviewed for clear error. 35 U.S.C.A. § 103.

[2] Patents 291 ⚿32

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k31 Evidence of Invention
291k32 k. Presumptions and Burden of Proof. Most Cited Cases
Patent examiner bears burden of establishing prima facie case of obviousness; only if this burden is met does burden of coming forward with rebuttal argument or evidence shift to applicant. 35 U.S.C.A. § 103.

[3] Patents 291 ⚿36(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k36 Weight and Sufficiency
291k36(1) k. In General. Most Cited Cases

Patents 291 ⚿324.55(4)

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k324 Appeal
291k324.55 Questions of Fact, Verdicts, and Findings
291k324.55(3) Issues of Validity
291k324.55(4) k. Novelty, In-

vention, Anticipation, and Obviousness. Most Cited Cases
When references cited by patent examiner fail to establish prima facie case of obviousness, rejection on ground of obviousness is improper and will be overturned. 35 U.S.C.A. § 103.

[4] Patents 291 ⚿16.3

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.3 k. Natural or Scientific Phenomena or Principles. Most Cited Cases

Patents 291 ⚿16.25

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical Compounds. Most Cited Cases
Combination of prior art reference teaching method of gene cloning, together with reference disclosing partial amino acid sequence for a protein that stimulated cell division, did not render deoxyribonucleic acid (DNA) and complementary DNA (cDNA) molecules encoding protein prima facie obvious; prior art did not disclose any relevant cDNA molecules, let alone close relatives of specific, structurally defined cDNA molecules of patent claims. 35 U.S.C.A. § 103.

[5] Patents 291 ⚿16.3

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.3 k. Natural or Scientific Phenomena or Principles. Most Cited Cases

Patents 291 ⚿16.25

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical Compounds. Most Cited Cases
Prior art disclosure of amino acid sequence of protein does not necessarily render particular deoxyribonucleic acid (DNA) molecules encoding protein obvious because redundancy of genetic code permits one to hypothesizing enormous number of DNA sequences coding for the protein; no particular one of these DNAs can be obvious unless there is something in prior art to lead to particular DNA and indicate that it should be prepared. 35 U.S.C.A. § 103.

[6] Patents 291 ⚿16.25

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical Compounds. Most Cited Cases
Existence of general method of isolating complementary deoxyribonucleic acid (cDNA) or DNA molecules is essentially irrelevant to question of whether specific molecules themselves would have been obvious, in absence of other prior art that suggests claimed DNAs. 35 U.S.C.A. § 103.

[7] Patents 291 ⚿26(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k26 Combination
291k26(1) k. In General. Most Cited Cases
Where there is prior art that suggests claimed compound, existence, or lack thereof, of enabling process for making that compound is factor in any patentability determination; there must, however, still be prior art that suggests claimed compound in order for prima facie case of obviousness to be made out. 35 U.S.C.A. § 103.

[8] Patents 291 ⚿16(1)

291 Patents
291II Patentability

291II(A) Invention; Obviousness
291k16 Invention and Obviousness in General
291k16(1) k. In General. Most Cited Cases
General incentive does not make obvious particular result, nor does existence of techniques by which to make those efforts to be carried out. 35 U.S.C.A. § 103.

[9] Patents 291 ⚿26(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k26 Combination
291k26(1) k. In General. Most Cited Cases
Fact that one can conceive general process in advance for preparing undefined compound does not mean that claimed specific compound was precisely envisioned and therefore obvious. 35 U.S.C.A. § 103.

[10] Patents 291 ⚿26(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k26 Combination
291k26(1) k. In General. Most Cited Cases
Conceived method of preparing some unidentified deoxyribonucleic acid (DNA) does not define it with precision necessary to render it obvious over protein it encodes. 35 U.S.C.A. § 103.

[11] Patents 291 ⚿26(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k26 Combination
291k26(1) k. In General. Most Cited Cases
Patent claims generically encompassing all deoxyribonucleic acid (DNA) sequences encoding human and bovine protein to stimulate cell division were not invalid as obvious, where prior art disclosed only partial amino acid sequence for the protein. 35 U.S.C.A. § 103.

***1553** G. Harley Blosser,Senniger, Powers, Leavitt & Roedel, of St. Louis, MO, argued for appellants. With him on the brief was Donald G. Leavitt.
Donald S. Chisum, Morrison & Foerster, Seattle, WA, argued for amicus curiae, The Biotechnology Industry Ass'n and The Bay Area Bioscience Center. With him on the brief were Debra A. Shetka, Morrison & Forester, Palo Alto, CA and Robert P. Blackburn, Emeryville, CA.
Teddy S. Gron, Acting Associate Sol., Arlington, VA, argued for appellee. With him on the brief was Albin F. Drost, Acting Sol. Nancy J. Linck, Office of the Sol., Arlington, VA, represented appellee.

Before ARCHER, Chief Judge, NIES and LOURIE, Circuit Judges.

LOURIE, Circuit Judge.
Thomas F. Deuel, Yue-Sheng Li, Ned R. Siegel, and Peter G. Milner (collectively "Deuel") appeal from the November 30, 1993 decision of the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences affirming the examiner's final rejection of claims 4-7 of application Serial No. 07/542,232, entitled "Heparin-Binding ***1554** Growth Factor," as unpatentable on the ground of obviousness under 35 U.S.C. § 103 (1988). *Ex parte Deuel,* 33 USPQ2d 1445 (Bd.Pat.App.Int.1993). Because the Board erred in concluding that Deuel's claims 5 and 7 directed to specific cDNA molecules would have been obvious in light of the applied references, and no other basis exists in the record to support the rejection with respect to claims 4 and 6 generically covering all possible DNA molecules coding for the disclosed proteins, we reverse.

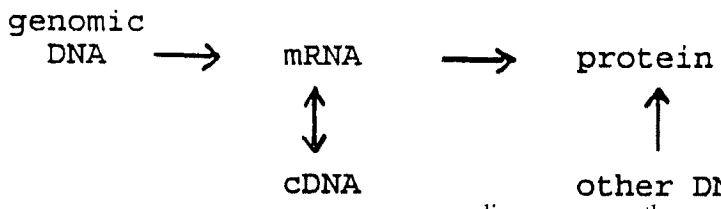
BACKGROUND

The claimed invention relates to isolated and purified DNA and cDNA molecules encoding heparin-binding growth factors ("HBGFs").[FN1] HBGFs are proteins that stimulate mitogenic activity (cell division) and thus facilitate the repair or replacement of damaged or diseased tissue. DNA (deoxyribonucleic acid) is a generic term which encompasses an enormous number of complex macromolecules made up of nucleotide units. DNAs consist of four different nucleotides containing the nitrogenous bases adenine, guanine, cytosine, and thymine. A sequential grouping of three such nucleotides (a "codon") codes for one amino acid. A DNA's sequence of codons thus determines the sequence of amino acids assembled during protein synthesis. Since there are 64 possible codons, but only 20 natural amino acids, most amino acids are coded for by more than one codon. This is referred to as the "redundancy" or "degeneracy" of the genetic code.

FN1. For a more extensive discussion of recombinant DNA technology, *see In re O'Farrell,* 853 F.2d 894, 895-99, 7 USPQ2d 1673, 1674-77 (Fed.Cir.1988); *Amgen Inc. v. Chugai Pharmaceutical Co.,* 927 F.2d 1200, 18 USPQ2d 1016 (Fed.Cir.), *cert. denied,* 502 U.S. 856, 112 S.Ct. 169, 116 L.Ed.2d 132 (1991).

DNA functions as a blueprint of an organism's genetic information. It is the major component of genes, which are located on chromosomes in the cell nucleus. Only a small part of chromosomal DNA encodes functional proteins.

Messenger ribonucleic acid ("mRNA") is a similar molecule that is made or transcribed from DNA as part of the process of protein synthesis. Complementary DNA ("cDNA") is a complementary copy ("clone") of mRNA, made in the laboratory by reverse transcription of mRNA. Like mRNA, cDNA contains only the protein-encoding regions of DNA. Thus, once a cDNA's nucleotide sequence is known, the amino acid sequence of the protein for which it codes may be predicted using the genetic code relationship between codons and amino acids. The reverse is not true, however, due to the degeneracy of the code. Many other DNAs may code for a particular protein. The functional relationships between DNA, mRNA, cDNA, and a protein may conveniently be expressed as follows:



Collections ("libraries") of DNA and cDNA molecules derived from various species may be constructed in the laboratory or obtained from commercial sources. Complementary DNA libraries contain a mixture of cDNA clones reverse-transcribed from the mRNAs found in a specific tissue source. Complementary DNA libraries are tissue-specific because proteins and their corresponding mRNAs are only made ("expressed") in specific tissues, depending upon the protein. Genomic DNA ("gDNA") libraries, by contrast, theoretically contain all of a species' chromosomal DNA. The molecules present in cDNA and DNA libraries may be of unknown function and chemical structure, and ***1555** the proteins which they encode may be unknown. However, one may attempt to retrieve molecules of interest from cDNA or gDNA libraries by screening such libraries with a gene probe, which is a synthetic radiolabelled nucleic acid sequence designed to bond ("hybridize") with a target complementary base sequence. Such "gene cloning" tech-

niques thus exploit the fact that the bases in DNA always hybridize in complementary pairs: adenine bonds with thymine and guanine bonds with cytosine. A gene probe for potentially isolating DNA or cDNA encoding a protein may be designed once the protein's amino acid sequence, or a portion thereof, is known.

As disclosed in Deuel's patent application, Deuel isolated and purified HBGF from bovine uterine tissue, found that it exhibited mitogenic activity, and determined the first 25 amino acids of the protein's N-terminal sequence.[FN2] Deuel then isolated a cDNA molecule encoding bovine uterine HBGF by screening a bovine uterine cDNA library with an oligonucleotide probe designed using the experimentally determined N-terminal sequence of the HBGF. Deuel purified and sequenced the cDNA molecule, which was found to consist of a sequence of 1196 nucleotide base pairs. From the cDNA's nucleotide sequence, Deuel then predicted the complete amino acid sequence of bovine uterine HBGF disclosed in Deuel's application.

> FN2. Deuel determined that the N-terminal sequence of bovine uterus HBGF is Gly- Lys- Lys- Glu- Lys- Pro- Glu- Lys- Lys- Val- Lys- Lys- Ser- Asp- Cys- Gly- Glu-Trp-Gln-Trp-Ser-Val-Cys-Val-Pro.

Deuel also isolated a cDNA molecule encoding human placental HBGF by screening a human placental cDNA library using the isolated bovine uterine cDNA clone as a probe. Deuel purified and sequenced the human placental cDNA clone, which was found to consist of a sequence of 961 nucleotide base pairs. From the nucleotide sequence of the cDNA molecule encoding human placental HBGF, Deuel predicted the complete amino acid sequence of human placental HBGF disclosed in Deuel's application. The predicted human placental and bovine uterine HBGFs each have 168 amino acids and calculated molecular weights of 18.9 kD. Of the 168 amino acids present in the two HBGFs discovered by Deuel, 163 are identical. Deuel's application does not describe the chemical structure of, or state how to isolate and purify, any DNA or cDNA molecule except the disclosed human placental and bovine uterine cDNAs, which are the subject of claims 5 and 7.

Claims 4-7 on appeal are all independent claims and read, in relevant part, as follows:

> 4. A purified and isolated DNA sequence consisting of a sequence encoding human heparin binding growth factor of 168 amino acids having the following amino acid sequence: Met Gln Ala ... [remainder of 168 amino acid sequence].
>
> 5. The purified and isolated cDNA of human heparin-binding growth factor having the following nucleotide sequence: GTCAAAGGCA ... [remainder of 961 nucleotide sequence].
>
> 6. A purified and isolated DNA sequence consisting of a sequence encoding bovine heparin binding growth factor of 168 amino acids having the following amino acid sequence: Met Gln Thr ... [remainder of 168 amino acid sequence].
>
> 7. The purified and isolated cDNA of bovine heparin-binding growth factor having the following nucleotide sequence: GAGTGGAGAG ... [remainder of 1196 nucleotide sequence].

Claims 4 and 6 generically encompass *all* isolated/purified DNA sequences (natural and synthetic) encoding human and bovine HBGFs, despite the fact

that Deuel's application does not describe the chemical structure of, or tell how to obtain, any DNA or cDNA except the two disclosed cDNA molecules. Because of the redundancy of the genetic code, claims 4 and 6 each encompass an enormous number of DNA molecules, including the isolated/purified chromosomal DNAs encoding the human and bovine proteins. Claims 5 and 7, on the other hand, are directed to the specifically disclosed cDNA molecules encoding human and bovine HBGFs, respectively.

During prosecution, the examiner rejected claims 4-7 under 35 U.S.C. § 103 as unpatentable over the combined teachings of Bohlen***1556** [FN3]] and Maniatis.[FN4] The Bohlen reference discloses a group of protein growth factors designated as heparin-binding brain mitogens ("HBBMs") useful in treating burns and promoting the formation, maintenance, and repair of tissue, particularly neural tissue. Bohlen isolated three such HBBMs from human and bovine brain tissue. These proteins have respective molecular weights of 15 kD, 16 kD, and 18 kD. Bohlen determined the first 19 amino acids of the proteins' N-terminal sequences, which were found to be identical for human and bovine HBBMs.[FN5] Bohlen teaches that HBBMs are brain-specific, and suggests that the proteins may be homologous between species. The reference provides no teachings concerning DNA or cDNA coding for HBBMs.

> FN3. European Patent Application No. 0326075, naming Peter Bohlen as inventor, published August 2, 1989.
>
> FN4. Maniatis et al., *Molecular Cloning: A Laboratory Manual,*"Screening Bacteriophage [lambda] Libraries for Specific DNA Sequences by Recombination in *Escherichia coli,*" Cold Spring Harbor Laboratory, New York, 1982, pp. 353-361.
>
> FN5. Bohlen's disclosed N-terminal sequence for human and bovine HBBMs is Gly-Lys- Lys- Glu- Lys- Pro- Glu- Lys- Lys- Val-Lys-Lys-Ser-Asp-Cys-Gly-Glu-Trp-Gln.
> This sequence matches the first 19 amino acids of Deuel's disclosed N-terminal sequence.

Maniatis describes a method of isolating DNAs or cDNAs by screening a DNA or cDNA library with a gene probe. The reference outlines a general technique for cloning a gene; it does not describe how to isolate a particular DNA or cDNA molecule. Maniatis does not discuss certain steps necessary to isolate a target cDNA, *e.g.,* selecting a tissue-specific cDNA library containing a target cDNA and designing an oligonucleotide probe that will hybridize with the target cDNA.

The examiner asserted that, given Bohlen's disclosure of a heparin-binding protein and its N-terminal sequence and Maniatis's gene cloning method, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to clone a gene for HBGF.[FN6] According to the examiner, Bohlen's published N-terminal sequence would have motivated a person of ordinary skill in the art to clone such a gene because cloning the gene would allow recombinant production of HBGF, a useful protein. The examiner reasoned that a person of ordinary skill in the art could have designed a gene probe based on Bohlen's disclosed N-terminal sequence, then screened a DNA library in accordance with Maniatis's gene cloning method to isolate a gene encoding an HBGF. The examiner did not distinguish between claims 4 and 6 generically directed to all DNA sequences encoding human and bovine HBGFs and claims 5 and 7 reciting particular cDNAs.

> FN6. The examiner and the Board apparently used the term "gene" to refer both to natural (chromosomal) DNA and synthetic cDNA. We will use the several terms as appropriate.

In reply, Deuel argued, *inter alia,* that Bohlen teaches away from the claimed cDNA molecules because Bohlen suggests that HBBMs are brain-specific and, thus, a person of ordinary skill in the art would not have tried to isolate corresponding cDNA clones from human placental and bovine uterine cDNA libraries. The examiner made the rejection final, however, asserting that

> [t]he starting materials are not relevant in this case, because it was well known in the art at the time the invention was made that proteins, especially the general class of heparin binding proteins, are highly homologous between species and tissue type. It would have been entirely obvious to attempt to isolate a known protein from different tissue types and even different species.

No prior art was cited to support the proposition that it would have been obvious to screen human placental and bovine uterine cDNA libraries for the claimed cDNA clones. Presumably, the examiner was relying on Bohlen's suggestion that HBBMs may be homologous between species, although the examiner did not explain how homology between species suggests homology between tissue types.

The Board affirmed the examiner's final rejection. In its opening remarks, the Board noted that it is "constantly advised by the ***1557** patent examiners, who are highly skilled in this art, that cloning procedures are routine in the art." According to the Board, "the examiners urge that when the sequence of a protein is placed into the public domain, the gene is also placed into the public domain because of the routine nature of cloning techniques." Addressing the rejection at issue, the Board determined that Bohlen's disclosure of the existence and isolation of HBBM, a functional protein, would also advise a person of ordinary skill in the art that a gene exists encoding HBBM. The Board found that a person of ordinary skill in the art would have been motivated to isolate such a gene because the protein has useful mitogenic properties, and isolating the gene for HBBM would permit large quantities of the protein to be produced for study and possible commercial use. Like the examiner, the Board asserted, without explanation, that HBBMs are the same as HBGFs and that the genes encoding these proteins are identical. The Board concluded that "the Bohlen reference would have suggested to those of ordinary skill in this art that they should make the gene, and the Maniatis reference would have taught a technique for 'making' the gene with a reasonable expectation of success." Responding to Deuel's argument that the claimed cDNA clones were isolated from human placental and bovine uterine cDNA libraries, whereas the combined teachings of Bohlen and Maniatis would only have suggested screening a brain tissue cDNA library, the Board stated that "the claims before us are directed to the product and not the method of isolation. Appellants have not shown that the claimed DNA was not present in and could not have been readily isolated from the brain tissue utilized by Bohlen." Deuel now appeals.[FN7]

> FN7. Deuel is supported in its appeal by an *amicus curiae* brief submitted by the Biotechnology Industry Organization and the Bay Area Science Center. Amici urge that, contrary to controlling precedent, the PTO has unlawfully adopted a *per se* rule that a gene is *prima facie* obvious when at least part of the amino acid sequence of the protein encoded by the gene is known in the prior art.

DISCUSSION

[1][2][3] Obviousness is a question of law, which we review *de novo,* though factual findings underlying the Board's obviousness determination are reviewed for clear error. *In re Vaeck,* 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed.Cir.1991); *In re Woodruff,* 919 F.2d 1575, 1577, 16 USPQ2d 1934,

1935 (Fed.Cir.1990). The examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert,* 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed.Cir.1993); *In re Oetiker,* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed.Cir.1992). Only if this burden is met does the burden of coming forward with rebuttal argument or evidence shift to the applicant. *Rijckaert,* 9 F.3d at 1532, 28 USPQ2d at 1956. When the references cited by the examiner fail to establish a *prima facie* case of obviousness, the rejection is improper and will be overturned. *In re Fine,* 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed.Cir.1988).

[4] On appeal, Deuel challenges the Board's determination that the applied references establish a *prima facie* case of obviousness. In response, the PTO maintains that the claimed invention would have been *prima facie* obvious over the combined teachings of Bohlen and Maniatis. Thus, the appeal raises the important question whether the combination of a prior art reference teaching a method of gene cloning, together with a reference disclosing a partial amino acid sequence of a protein, may render DNA and cDNA molecules encoding the protein *prima facie* obvious under § 103.

Deuel argues that the PTO failed to follow the proper legal standard in determining that the claimed cDNA molecules would have been *prima facie* obvious despite the lack of structurally similar compounds in the prior art. Deuel argues that the PTO has not cited a reference teaching cDNA molecules, but instead has improperly rejected the claims based on the alleged obviousness of a method of making the molecules. We agree.

Because Deuel claims new chemical entities in structural terms, a *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art. ***1558** Normally a *prima facie* case of obviousness is based upon structural similarity, *i.e.,* an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties. Similarly, a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (*e.g.,* ortho v. para).

In all of these cases, however, the prior art teaches a specific, structurally-definable compound and the question becomes whether the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention. *See In re Jones,* 958 F.2d 347, 351, 21 USPQ2d 1941, 1944 (Fed.Cir.1992); *In re Dillon,* 919 F.2d 688, 692, 16 USPQ2d 1897, 1901 (Fed.Cir.1990) (en banc) ("structural similarity between claimed and prior art subject matter, ... where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness"), *cert. denied,* 500 U.S. 904, 111 S.Ct. 1682, 114 L.Ed.2d 77 (1991); *In re Grabiak,* 769 F.2d 729, 731-32, 226 USPQ 870, 872 (Fed.Cir.1985) ("[I]n the case before us there must be adequate support in the prior art for the [prior art] ester/[claimed] thioester change in structure, in order to complete the PTO's *prima facie* case and shift the burden of going forward to the applicant."); *In re Lalu,* 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed.Cir.1984) ("The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound.").

Here, the prior art does not disclose any relevant cDNA molecules, let alone close relatives of the specific, structurally-defined cDNA molecules of claims 5 and 7 that might render them obvious. Maniatis suggests an allegedly obvious process for trying to isolate cDNA molecules, but that, as we will indicate below, does not fill the gap regarding the subject matter of claims 5 and 7. Further, while

the general idea of the claimed molecules, their function, and their general chemical nature may have been obvious from Bohlen's teachings, and the knowledge that some gene existed may have been clear, the precise cDNA molecules of claims 5 and 7 would not have been obvious over the Bohlen reference because Bohlen teaches proteins, not the claimed or closely related cDNA molecules. The redundancy of the genetic code precluded contemplation of or focus on the specific cDNA molecules of claims 5 and 7. Thus, one could not have conceived the subject matter of claims 5 and 7 based on the teachings in the cited prior art because, until the claimed molecules were actually isolated and purified, it would have been highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained. What cannot be contemplated or conceived cannot be obvious.

The PTO's theory that one might have been motivated to try to do what Deuel in fact accomplished amounts to speculation and an impermissible hindsight reconstruction of the claimed invention. It also ignores the fact that claims 5 and 7 are limited to specific compounds, and any motivation that existed was a general one, to try to obtain a gene that was yet undefined and may have constituted many forms. A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search. More is needed and it is not found here.

[5] The genetic code relationship between proteins and nucleic acids does not overcome the deficiencies of the cited references. A prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein. No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be ***1559** prepared. We recently held in *In re Baird,* 16 F.3d 380, 29 USPQ2d 1550 (Fed.Cir.1994), that a broad genus does not necessarily render obvious each compound within its scope. Similarly, knowledge of a protein does not give one a conception of a particular DNA encoding it. Thus, *a fortiori,* Bohlen's disclosure of the N-terminal portion of a protein, which the PTO urges is the same as HBGF, would not have suggested the particular cDNA molecules defined by claims 5 and 7. This is so even though one skilled in the art knew that some DNA, albeit not in purified and isolated form, did exist. The compounds of claims 5 and 7 are specific compounds not suggested by the prior art. A different result might pertain, however, if there were prior art, *e.g.,* a protein of sufficiently small size and simplicity, so that lacking redundancy, each possible DNA would be obvious over the protein. *See In re Petering,* 301 F.2d 676 (CCPA 1962) (prior art reference disclosing limited genus of 20 compounds rendered every species within the genus unpatentable). That is not the case here.

The PTO's focus on known methods for potentially isolating the claimed DNA molecules is also misplaced because the claims at issue define compounds, not methods. *See In re Bell,* 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed.Cir.1993). In *Bell,* the PTO asserted a rejection based upon the combination of a primary reference disclosing a protein (*and its complete amino acid sequence*) with a secondary reference describing a general method of gene cloning. We reversed the rejection, holding in part that "[t]he PTO's focus on Bell's method is misplaced. Bell does not claim a method. Bell claims compositions, and the issue is the obviousness of the claimed compositions, not of the method by which they are made." *Id.*

[6][7][8] We today reaffirm the principle, stated in *Bell,* that the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed

DNAs. A prior art disclosure of a process *reciting a particular compound* or obvious variant thereof as a product of the process is, of course, another matter, raising issues of anticipation under 35 U.S.C. § 102 as well as obviousness under § 103. Moreover, where there is prior art that suggests a claimed compound, the existence, or lack thereof, of an enabling process for making that compound is surely a factor in any patentability determination. *See In re Brown,* 329 F.2d 1006, 141 USPQ 245 (CCPA 1964) (reversing rejection for lack of an enabling method of making the claimed compound). There must, however, still be prior art that suggests the claimed compound in order for a *prima facie* case of obviousness to be made out; as we have already indicated, that prior art was lacking here with respect to claims 5 and 7. Thus, even if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein's structure, might have provided motivation to prepare *a* cDNA or made it obvious to prepare *a* cDNA, that does not necessarily make obvious a particular claimed cDNA. "Obvious to try" has long been held not to constitute obviousness. *In re O'Farrell,* 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed.Cir.1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. Thus, Maniatis's teachings, even in combination with Bohlen, fail to suggest the claimed invention.

[9][10] The PTO argues that a compound may be defined by its process of preparation and therefore that a conceived process for making or isolating it provides a definition for it and can render it obvious. It cites *Amgen Inc. v. Chugai Pharmaceutical Co.,* 927 F.2d 1200, 18 USPQ2d 1016 (Fed.Cir.), *cert. denied,* 502 U.S. 856, 112 S.Ct. 169, 116 L.Ed.2d 132 (1991), for that proposition. We disagree. The fact that one can conceive a general process in advance for preparing an *undefined* compound does not mean that a claimed *specific* compound was precisely envisioned and therefore obvious. A substance may indeed be defined by its process of preparation. That occurs, however, when it has already been prepared by that process and one therefore knows that the result of that process is the stated compound. The process is part of the definition of the compound.***1560** But that is not possible in advance, especially when the hypothetical process is only a general one. Thus, a conceived method of preparing some undefined DNA does not define it with the precision necessary to render it obvious over the protein it encodes. We did not state otherwise in *Amgen. See Amgen,* 927 F.2d at 1206-09, 18 USPQ2d at 1021-23 (isolated/purified human gene held nonobvious; no conception of gene without envisioning its precise identity despite conception of general process of preparation).

We conclude that, because the applied references do not teach or suggest the claimed cDNA molecules, the final rejection of claims 5 and 7 must be reversed. *See also Bell,* 991 F.2d at 784-85, 26 USPQ2d at 1531-32 (human DNA sequences encoding IGF proteins nonobvious over asserted combination of references showing gene cloning method and complete amino acid sequences of IGFs).

[11] Claims 4 and 6 are of a different scope than claims 5 and 7. As is conceded by Deuel, they generically encompass all DNA sequences encoding human and bovine HBGFs. Written in such a result-oriented form, claims 4 and 6 are thus tantamount to the general idea of all genes encoding the protein, all solutions to the problem. Such an idea might have been obvious from the *complete* amino acid sequence of the protein, coupled with knowledge of the genetic code, because this information may have enabled a person of ordinary skill in the art to envision the idea of, and, perhaps with the aid of a computer, even identify all members of the claimed genus. The Bohlen reference, however, only discloses a partial amino acid sequence, and thus it appears that, based on the above analysis, the claimed genus would not have been obvious over this prior art disclosure. We will therefore also reverse the final rejection of claims 4 and 6 because neither the Board nor the patent examiner articu-

lated any separate reasons for holding these claims unpatentable apart from the grounds discussed above.

One further matter requires comment. Because Deuel's patent application does not describe how to obtain any DNA except the disclosed cDNA molecules, claims 4 and 6 may be considered to be inadequately supported by the disclosure of the application. *See generally Amgen Inc. v. Chugai Pharmaceutical Co.,* 927 F.2d 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed.Cir.) (generic DNA sequence claims held invalid under 35 U.S.C. § 112, first paragraph), *cert. denied,* 502 U.S. 856, 112 S.Ct. 169, 116 L.Ed.2d 132 (1991); *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (Section 112"requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). As this issue is not before us, however, we will not address whether claims 4 and 6 satisfy the enablement requirement of § 112, first paragraph, but will leave to the PTO the question whether any further rejection is appropriate.

We have considered the PTO's remaining arguments and find them not persuasive.

CONCLUSION

The Board's decision affirming the final rejection of claims 4-7 is reversed.

REVERSED

C.A.Fed.,1995.
In re Deuel
51 F.3d 1552, 63 USLW 2624, 34 U.S.P.Q.2d 1210

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Westlaw

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127 S.Ct. 1727, 167 L.Ed.2d 705, 75 USLW 4289, 82 U.S.P.Q.2d 1385, 07 Cal. Daily Op. Serv. 4654, 20 Fla. L. Weekly Fed. S 248

Supreme Court of the United States
KSR INTERNATIONAL CO., Petitioner,
v.
TELEFLEX INC. et al.
No. 04-1350.

Argued Nov. 28, 2006.
Decided April 30, 2007.

Background: Exclusive licensee of patent for position-adjustable vehicle pedal assembly sued competitor for infringement. The United States District Court for the Eastern District of Michigan, 298 F.Supp.2d 581, granted summary judgment for competitor on the ground of obviousness. Licensee appealed. The United States Court of Appeals for the Federal Circuit, 119 Fed.Appx. 282, reversed. Certiorari was granted.

Holding: The Supreme Court, Justice Kennedy, held that patent was invalid as obvious.

Reversed and remanded.

West Headnotes

[1] Patents 291 ⚿26(1.1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k26 Combination
291k26(1.1) k. Use of Old or Well-Known Elements. Most Cited Cases
Patent claiming the combination of elements of prior art is obvious if the improvement is no more than the predictable use of prior art elements according to their established functions. 35 U.S.C.A. § 103.

[2] Patents 291 ⚿26(1.1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k26 Combination
291k26(1.1) k. Use of Old or Well-Known Elements. Most Cited Cases
Patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. 35 U.S.C.A. § 103.

[3] Patents 291 ⚿16.5(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.5 State of Prior Art and Advancement Therein
291k16.5(1) k. In General. Most Cited Cases
In determining whether subject matter of patent claim is obvious, neither the particular motivation nor the avowed purpose of patentee controls; what matters is the objective reach of the claim. 35 U.S.C.A. § 103.

[4] Patents 291 ⚿16.5(4)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.5 State of Prior Art and Advancement Therein
291k16.5(4) k. Remedying Defects or Solving Problems. Most Cited Cases
Patent's subject matter can be proved obvious by noting that there existed at time of invention a known problem for which there was an obvious solution encompassed by patent's claims. 35 U.S.C.A. § 103.

[5] Patents 291 ⚿16(3)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16 Invention and Obviousness in

General
291k16(3) k. View of Person Skilled in Art. Most Cited Cases

Patents 291 ⚿16.5(4)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.5 State of Prior Art and Advancement Therein
291k16.5(4) k. Remedying Defects or Solving Problems. Most Cited Cases
In determining whether patent combining known elements is obvious, question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art; under correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide reason for combining the elements in the manner claimed. 35 U.S.C.A. § 103.

[6] Patents 291 ⚿16.5(4)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.5 State of Prior Art and Advancement Therein
291k16.5(4) k. Remedying Defects or Solving Problems. Most Cited Cases

Patents 291 ⚿17(1)

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k17 Nature and Degree of Skill Involved
291k17(1) k. In General. Most Cited Cases
When there is design need or market pressure to solve a problem and there are finite number of identified, predictable solutions, person of ordinary skill has good reason to pursue the known options within his or her technical grasp, and if this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense; in that instance, the fact that a combination was obvious to try might show that patent for it was obvious. 35 U.S.C.A. § 103.

[7] Patents 291 ⚿16.22

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.22 k. Automobiles and Vehicles. Most Cited Cases
Patent claim disclosing position-adjustable pedal assembly with electronic pedal position sensor attached to support member of pedal assembly was invalid as obvious, in view of patent for adjustable pedal with a fixed pivot, and patent teaching a solution to wire chafing problems, namely locating the sensor on support structure; it was obvious to person of ordinary skill in the art to combine first patent with pivot-mounted pedal position sensor. 35 U.S.C.A. § 103.

[8] Patents 291 ⚿323.2(2)

291 Patents
291XII Infringement
291XII(C) Suits in Equity
291k323 Final Judgment or Decree
291k323.2 Summary Judgment
291k323.2(2) k. Presence or Absence of Fact Issues. Most Cited Cases
Where content of prior art, scope of patent claim, and level of ordinary skill in the art are not in material dispute, and obviousness of claim is apparent in light of these factors, summary judgment is appropriate. 35 U.S.C.A. § 103.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated

291k328(2) k. Original Utility. Most Cited Cases
5,010,782, 5,063,811, 5,241,936, 5,385,068, 5,460,061, 5,819,593, 6,151,976. Cited as Prior Art.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases
6,109,241. Cited.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases
6,237,565. Invalid.

***1728** *Syllabus* [FN*]

FN* The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States v. Detroit Timber & Lumber Co.,* 200 U.S. 321, 337, 26 S.Ct. 282, 50 L.Ed. 499.

To control a conventional automobile's speed, the driver depresses or releases the gas pedal, which interacts with the throttle via a cable or other mechanical link. Because the pedal's position in the footwell normally cannot be adjusted, a driver wishing to be closer or farther from it must either reposition himself in the seat ***1729** or move the seat, both of which can be imperfect solutions for smaller drivers in cars with deep footwells. This prompted inventors to design and patent pedals that could be adjusted to change their locations. The Asano patent reveals a support structure whereby, when the pedal location is adjusted, one of the pedal's pivot points stays fixed. Asano is also designed so that the force necessary to depress the pedal is the same regardless of location adjustments. The Redding patent reveals a different, sliding mechanism where both the pedal and the pivot point are adjusted.

In newer cars, computer-controlled throttles do not operate through force transferred from the pedal by a mechanical link, but open and close valves in response to electronic signals. For the computer to know what is happening with the pedal, an electronic sensor must translate the mechanical operation into digital data. Inventors had obtained a number of patents for such sensors. The so-called '936 patent taught that it was preferable to detect the pedal's position in the pedal mechanism, not in the engine, so the patent disclosed a pedal with an electronic sensor on a pivot point in the pedal assembly. The Smith patent taught that to prevent the wires connecting the sensor to the computer from chafing and wearing out, the sensor should be put on a fixed part of the pedal assembly rather than in or on the pedal's footpad. Inventors had also patented self-contained modular sensors, which can be taken off the shelf and attached to any mechanical pedal to allow it to function with a computer-controlled throttle. The '068 patent disclosed one such sensor. Chevrolet also manufactured trucks using modular sensors attached to the pedal support bracket, adjacent to the pedal and engaged with the pivot shaft about which the pedal rotates. Other patents disclose electronic sensors attached to adjustable pedal assemblies. For example, the Rixon patent locates the sensor in the pedal footpad, but is known for wire chafing.

After petitioner KSR developed an adjustable pedal system for cars with cable-actuated throttles and obtained its '976 patent for the design, General Motors Corporation (GMC) chose KSR to supply adjustable pedal systems for trucks using computer-controlled throttles. To make the '976 pedal compatible with the trucks, KSR added a modular sensor to its design. Respondents (Teleflex) hold the exclusive license for the Engelgau patent, claim

4 of which discloses a position-adjustable pedal assembly with an electronic pedal position sensor attached a fixed pivot point. Despite having denied a similar, broader claim, the U.S. Patent and Trademark Office (PTO) had allowed claim 4 because it included the limitation of a fixed pivot position, which distinguished the design from Redding's. Asano was neither included among the Engelgau patent's prior art references nor mentioned in the patent's prosecution, and the PTO did not have before it an adjustable pedal with a fixed pivot point. After learning of KSR's design for GMC, Teleflex sued for infringement, asserting that KSR's pedal system infringed the Engelgau patent's claim 4. KSR countered that claim 4 was invalid under § 103 of the Patent Act, which forbids issuance of a patent when "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art."

Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18, 86 S.Ct. 684, 15 L.Ed.2d 545, set out an objective analysis for applying § 103: "[T]he scope and content of the prior art are ... determined; differences between the prior art and the ***1730** claims at issue are ... ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." While the sequence of these questions might be reordered in any particular case, the factors define the controlling inquiry. However, seeking to resolve the obviousness question with more uniformity and consistency, the Federal Circuit has employed a "teaching, suggestion, or motivation" (TSM) test, under which a patent claim is only proved obvious if the prior art, the problem's nature, or the knowledge of a person having ordinary skill in the art reveals some motivation or suggestion to combine the prior art teachings.

The District Court granted KSR summary judgment. After reviewing pedal design history, the Engelgau patent's scope, and the relevant prior art, the court considered claim 4's validity, applying *Graham's* framework to determine whether under summary-judgment standards KSR had demonstrated that claim 4 was obvious. The court found "little difference" between the prior art's teachings and claim 4: Asano taught everything contained in the claim except using a sensor to detect the pedal's position and transmit it to a computer controlling the throttle. That additional aspect was revealed in, *e.g.,* the '068 patent and Chevrolet's sensors. The court then held that KSR satisfied the TSM test, reasoning (1) the state of the industry would lead inevitably to combinations of electronic sensors and adjustable pedals, (2) Rixon provided the basis for these developments, and (3) Smith taught a solution to Rixon's chafing problems by positioning the sensor on the pedal's fixed structure, which could lead to the combination of a pedal like Asano with a pedal position sensor.

Reversing, the Federal Circuit ruled the District Court had not applied the TSM test strictly enough, having failed to make findings as to the specific understanding or principle within a skilled artisan's knowledge that would have motivated one with no knowledge of the invention to attach an electronic control to the Asano assembly's support bracket. The Court of Appeals held that the District Court's recourse to the nature of the problem to be solved was insufficient because, unless the prior art references addressed the precise problem that the patentee was trying to solve, the problem would not motivate an inventor to look at those references. The appeals court found that the Asano pedal was designed to ensure that the force required to depress the pedal is the same no matter how the pedal is adjusted, whereas Engelgau sought to provide a simpler, smaller, cheaper adjustable electronic pedal. The Rixon pedal, said the court, suffered from chafing but was not designed to solve that problem and

taught nothing helpful to Engelgau's purpose. Smith, in turn, did not relate to adjustable pedals and did not necessarily go to the issue of motivation to attach the electronic control on the pedal assembly's support bracket. So interpreted, the court held, the patents would not have led a person of ordinary skill to put a sensor on an Asano-like pedal. That it might have been obvious to try that combination was likewise irrelevant. Finally, the court held that genuine issues of material fact precluded summary judgment.

Held: The Federal Circuit addressed the obviousness question in a narrow, rigid manner that is inconsistent with § 103 and this Court's precedents. KSR provided ***1731** convincing evidence that mounting an available sensor on a fixed pivot point of the Asano pedal was a design step well within the grasp of a person of ordinary skill in the relevant art and that the benefit of doing so would be obvious. Its arguments, and the record, demonstrate that the Engelgau patent's claim 4 is obvious. Pp. 1739 - 1746.

1. *Graham* provided an expansive and flexible approach to the obviousness question that is inconsistent with the way the Federal Circuit applied its TSM test here. Neither § 103's enactment nor *Graham's* analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art. See *Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp.,* 340 U.S. 147, 152, 71 S.Ct. 127, 95 L.Ed. 162. Such a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. See, *e.g., United States v. Adams,* 383 U.S. 39, 50-52, 86 S.Ct. 708, 15 L.Ed.2d 572. When a work is available in one field, design incentives and other market forces can prompt variations of it, either in the same field or in another. If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, § 103 likely bars its patentability. Moreover, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions. Following these principles may be difficult if the claimed subject matter involves more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement. To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ. Pp. 1739 - 1741.

(b) The TSM test captures a helpful insight: A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art. Although common sense directs caution as to a patent application claiming as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the art to combine the elements as the new invention does. Inventions usually rely upon building blocks long since uncovered, and claimed discoveries almost necessarily will be combinations of what, in some sense, is already known. Helpful insights, however, need not become rigid and mandatory formulas. If it is so applied, the TSM test is incompatible with this Court's precedents. The diversity of inventive pursuits and of modern techno-

logy counsels against confining the obviousness analysis by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasizing the importance of published articles and the explicit ***1732** content of issued patents. In many fields there may be little discussion of obvious techniques or combinations, and market demand, rather than scientific literature, may often drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, for patents combining previously known elements, deprive prior inventions of their value or utility. Since the TSM test was devised, the Federal Circuit doubtless has applied it in accord with these principles in many cases. There is no necessary inconsistency between the test and the *Graham* analysis. But a court errs where, as here, it transforms general principle into a rigid rule limiting the obviousness inquiry. Pp. 1740 - 1741.

(c) The flaws in the Federal Circuit's analysis relate mostly to its narrow conception of the obviousness inquiry consequent in its application of the TSM test. The Circuit first erred in holding that courts and patent examiners should look only to the problem the patentee was trying to solve. Under the correct analysis, any need or problem known in the field and addressed by the patent can provide a reason for combining the elements in the manner claimed. Second, the appeals court erred in assuming that a person of ordinary skill in the art attempting to solve a problem will be led only to those prior art elements designed to solve the same problem. The court wrongly concluded that because Asano's primary purpose was solving the constant ratio problem, an inventor considering how to put a sensor on an adjustable pedal would have no reason to consider putting it on the Asano pedal. It is common sense that familiar items may have obvious uses beyond their primary purposes, and a person of ordinary skill often will be able to fit the teachings of multiple patents together like pieces of a puzzle. Regardless of Asano's primary purpose, it provided an obvious example of an adjustable pedal with a fixed pivot point, and the prior art was replete with patents indicating that such a point was an ideal mount for a sensor. Third, the court erred in concluding that a patent claim cannot be proved obvious merely by showing that the combination of elements was obvious to try. When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. Finally, the court drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. Rigid preventative rules that deny recourse to common sense are neither necessary under, nor consistent with, this Court's case law. Pp. 1741 - 1743.

2. Application of the foregoing standards demonstrates that claim 4 is obvious. Pp. 1743 - 1746.

(a) The Court rejects Teleflex's argument that the Asano pivot mechanism's design prevents its combination with a sensor in the manner claim 4 describes. This argument was not raised before the District Court, and it is unclear whether it was raised before the Federal Circuit. Given the significance of the District Court's finding that combining Asano with a pivot-mounted pedal position sensor fell within claim 4's scope, it is apparent that Teleflex would have made clearer challenges if it intended to preserve this claim. Its failure to clearly raise the argument, and the appeals court's silence on the issue, lead this Court to accept the District Court's conclusion. Pp. 1743 - 1744.

***1733** (b) The District Court correctly concluded that when Engelgau designed the claim 4 subject matter, it was obvious to a person of ordinary skill in the art to combine Asano with a pivot-mounted pedal position sensor. There then was a marketplace creating a strong incentive to convert mechanical pedals to electronic pedals, and the prior art taught a number of methods for doing so. The Fed-

eral Circuit considered the issue too narrowly by, in effect, asking whether a pedal designer writing on a blank slate would have chosen both Asano and a modular sensor similar to the ones used in the Chevrolet trucks and disclosed in the '068 patent. The proper question was whether a pedal designer of ordinary skill in the art, facing the wide range of needs created by developments in the field, would have seen an obvious benefit to upgrading Asano with a sensor. For such a designer starting with Asano, the question was where to attach the sensor. The '936 patent taught the utility of putting the sensor on the pedal device. Smith, in turn, explained not to put the sensor on the pedal footpad, but instead on the structure. And from Rixon's known wire-chafing problems, and Smith's teaching that the pedal assemblies must not precipitate any motion in the connecting wires, the designer would know to place the sensor on a nonmoving part of the pedal structure. The most obvious such point is a pivot point. The designer, accordingly, would follow Smith in mounting the sensor there. Just as it was possible to begin with the objective to upgrade Asano to work with a computer-controlled throttle, so too was it possible to take an adjustable electronic pedal like Rixon and seek an improvement that would avoid the wire-chafing problem. Teleflex has not shown anything in the prior art that taught away from the use of Asano, nor any secondary factors to dislodge the determination that claim 4 is obvious. Pp. 1744 - 1746.

3. The Court disagrees with the Federal Circuit's holding that genuine issues of material fact precluded summary judgment. The ultimate judgment of obviousness is a legal determination. *Graham,* 383 U.S., at 17, 86 S.Ct. 684. Where, as here, the prior art's content, the patent claim's scope, and the level of ordinary skill in the art are not in material dispute and the claim's obviousness is apparent, summary judgment is appropriate. Pp. 1745 - 1746.

119 Fed.Appx. 282, reversed and remanded.

KENNEDY, J., delivered the opinion for a unanimous Court.

James W. Dabney, for petitioner.
Thomas G. Hungar, for the United States as amicus curiae, by special leave of the Court, supporting the petitioner.
Thomas C. Goldstein, for respondents.
John F. Duffy, Fried, Frank, Harris, Shriver & Jacobson LLP, Of Counsel, James W. Dabney, Counsel of Record, New York, New York, Stephen S. Rabinowitz, Henry C. Lebowitz, Mitchell E. Epner, Darcy M. Goddard, Fried, Frank, Harris, Shriver & Jacobson LLP, New York, New York, Attorneys for Petitioner.
Kenneth C. Bass, III, Robert G. Sterne, Sterne, Kessler Goldstein & Fox P.L.L.C., Washington, DC, Rodger D. Young, Steven Susser, David Poirier, Young & Susser, P.C., Southfield, Thomas C. Goldstein, Counsel of Record, Michael A. O'Shea, Garreth A. Sarosi, Christopher R. Pudelski, Sarah C. Rispin, Akin Gump Strauss Hauer & Feld, LLP, Washington, DC, Samuel J. Haidle, David M. LaPrairie, Howard & Howard, Attorneys, P.C., Bloomfield Hills, MI, Tracy L. Casadio, ***1734** Elizabeth H. Rader, Akin Gump Strauss Hauer & Feld, LLP, Los Angeles, CA, Brief for the Respondents.For U.S. Supreme Court briefs, see:2006 WL 2515631 (Pet.Brief)2006 WL 2989549 (Resp.Brief)2006 WL 3367870 (Reply.Brief)2006 WL 3146709 (Resp.Supp.Brief)

Justice KENNEDY delivered the opinion of the Court.
Teleflex Incorporated and its subsidiary Technology Holding Company-both referred to here as Teleflex-sued KSR International Company for patent infringement. The patent at issue, United States Patent No. 6,237,565 B1, is entitled "Adjustable Pedal Assembly With Electronic Throttle Control." Supplemental App. 1. The patentee is Steven J. Engelgau, and the patent is referred to as "the Engelgau patent." Teleflex holds the exclusive license to the patent.

Claim 4 of the Engelgau patent describes a mechanism for combining an electronic sensor with an adjustable automobile pedal so the pedal's position

can be transmitted to a computer that controls the throttle in the vehicle's engine. When Teleflex accused KSR of infringing the Engelgau patent by adding an electronic sensor to one of KSR's previously designed pedals, KSR countered that claim 4 was invalid under the Patent Act, 35 U.S.C. § 103, because its subject matter was obvious.

Section 103 forbids issuance of a patent when "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains."

In *Graham v. John Deere Co. of Kansas City,* 383 U.S. 1, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966), the Court set out a framework for applying the statutory language of § 103, language itself based on the logic of the earlier decision in *Hotchkiss v. Greenwood,* 11 How. 248, 13 L.Ed. 683 (1851), and its progeny. See 383 U.S., at 15-17, 86 S.Ct. 684. The analysis is objective:

> "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Id.,* at 17-18, 86 S.Ct. 684.

While the sequence of these questions might be reordered in any particular case, the factors continue to define the inquiry that controls. If a court, or patent examiner, conducts this analysis and concludes the claimed subject matter was obvious, the claim is invalid under § 103.

Seeking to resolve the question of obviousness with more uniformity and consistency, the Court of Appeals for the Federal Circuit has employed an approach referred to by the parties as the "teaching, suggestion, or motivation" test (TSM test), under which a patent claim is only proved obvious if "some motivation or suggestion to combine the prior art teachings" can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art. See, *e.g., Al-Site Corp. v. VSI Int'l, Inc.,* 174 F.3d 1308, 1323-1324 (C.A.Fed.1999). KSR challenges that ***1735** test, or at least its application in this case. See 119 Fed.Appx. 282, 286-290 (C.A.Fed.2005). Because the Court of Appeals addressed the question of obviousness in a manner contrary to § 103 and our precedents, we granted certiorari, 547 U.S. ----, 126 S.Ct. 2965, 165 L.Ed.2d 949 (2006). We now reverse.

I

A

In car engines without computer-controlled throttles, the accelerator pedal interacts with the throttle via cable or other mechanical link. The pedal arm acts as a lever rotating around a pivot point. In a cable-actuated throttle control the rotation caused by pushing down the pedal pulls a cable, which in turn pulls open valves in the carburetor or fuel injection unit. The wider the valves open, the more fuel and air are released, causing combustion to increase and the car to accelerate. When the driver takes his foot off the pedal, the opposite occurs as the cable is released and the valves slide closed.

In the 1990's it became more common to install computers in cars to control engine operation. Computer-controlled throttles open and close valves in response to electronic signals, not through force transferred from the pedal by a mechanical link. Constant, delicate adjustments of air and fuel mixture are possible. The computer's rapid pro-

cessing of factors beyond the pedal's position improves fuel efficiency and engine performance.

For a computer-controlled throttle to respond to a driver's operation of the car, the computer must know what is happening with the pedal. A cable or mechanical link does not suffice for this purpose; at some point, an electronic sensor is necessary to translate the mechanical operation into digital data the computer can understand.

Before discussing sensors further we turn to the mechanical design of the pedal itself. In the traditional design a pedal can be pushed down or released but cannot have its position in the footwell adjusted by sliding the pedal forward or back. As a result, a driver who wishes to be closer or farther from the pedal must either reposition himself in the driver's seat or move the seat in some way. In cars with deep footwells these are imperfect solutions for drivers of smaller stature. To solve the problem, inventors, beginning in the 1970's, designed pedals that could be adjusted to change their location in the footwell. Important for this case are two adjustable pedals disclosed in U.S. Patent Nos. 5,010,782 (filed July 28, 1989) (Asano) and 5,460,061 (filed Sept. 17, 1993) (Redding). The Asano patent reveals a support structure that houses the pedal so that even when the pedal location is adjusted relative to the driver, one of the pedal's pivot points stays fixed. The pedal is also designed so that the force necessary to push the pedal down is the same regardless of adjustments to its location. The Redding patent reveals a different, sliding mechanism where both the pedal and the pivot point are adjusted.

We return to sensors. Well before Engelgau applied for his challenged patent, some inventors had obtained patents involving electronic pedal sensors for computer-controlled throttles. These inventions, such as the device disclosed in U.S. Patent No. 5,241,936 (filed Sept. 9, 1991) ('936), taught that it was preferable to detect the pedal's position in the pedal assembly, not in the engine. The '936 patent disclosed a pedal with an electronic sensor on a pivot point in the pedal assembly. U.S. Patent No. 5,063,811 (filed July 9, 1990) (Smith) taught that to prevent the ***1736** wires connecting the sensor to the computer from chafing and wearing out, and to avoid grime and damage from the driver's foot, the sensor should be put on a fixed part of the pedal assembly rather than in or on the pedal's footpad.

In addition to patents for pedals with integrated sensors inventors obtained patents for self-contained modular sensors. A modular sensor is designed independently of a given pedal so that it can be taken off the shelf and attached to mechanical pedals of various sorts, enabling the pedals to be used in automobiles with computer-controlled throttles. One such sensor was disclosed in U.S. Patent No. 5,385,068 (filed Dec. 18, 1992) ('068). In 1994, Chevrolet manufactured a line of trucks using modular sensors "attached to the pedal support bracket, adjacent to the pedal and engaged with the pivot shaft about which the pedal rotates in operation." 298 F.Supp.2d 581, 589 (E.D.Mich.2003).

The prior art contained patents involving the placement of sensors on adjustable pedals as well. For example, U.S. Patent No. 5,819,593 (filed Aug. 17, 1995) (Rixon) discloses an adjustable pedal assembly with an electronic sensor for detecting the pedal's position. In the Rixon pedal the sensor is located in the pedal footpad. The Rixon pedal was known to suffer from wire chafing when the pedal was depressed and released.

This short account of pedal and sensor technology leads to the instant case.

B

KSR, a Canadian company, manufactures and supplies auto parts, including pedal systems. Ford Motor Company hired KSR in 1998 to supply an adjustable pedal system for various lines of automobiles with cable-actuated throttle controls. KSR developed an adjustable mechanical pedal for Ford

and obtained U.S. Patent No. 6,151,976 (filed July 16, 1999) ('976) for the design. In 2000, KSR was chosen by General Motors Corporation (GMC or GM) to supply adjustable pedal systems for Chevrolet and GMC light trucks that used engines with computer-controlled throttles. To make the '976 pedal compatible with the trucks, KSR merely took that design and added a modular sensor.

Teleflex is a rival to KSR in the design and manufacture of adjustable pedals. As noted, it is the exclusive licensee of the Engelgau patent. Engelgau filed the patent application on August 22, 2000 as a continuation of a previous application for U.S. Patent No. 6,109,241, which was filed on January 26, 1999. He has sworn he invented the patent's subject matter on February 14, 1998. The Engelgau patent discloses an adjustable electronic pedal described in the specification as a "simplified vehicle control pedal assembly that is less expensive, and which uses fewer parts and is easier to package within the vehicle." Engelgau, col. 2, lines 2-5, Supplemental App. 6. Claim 4 of the patent, at issue here, describes:

> "A vehicle control pedal apparatus comprising:
> a support adapted to be mounted to a vehicle structure;
>
> an adjustable pedal assembly having a pedal arm moveable in for[e] and aft directions with respect to said support;
>
> a pivot for pivotally supporting said adjustable pedal assembly with respect to said support and defining a pivot axis; and
>
> an electronic control attached to said support for controlling a vehicle system;
>
> said apparatus characterized by said electronic control being responsive to said pivot for providing a signal that corresponds to pedal arm position as said pedal arm pivots about said pivot ***1737** axis between rest and applied positions wherein the position of said pivot remains constant while said pedal arm moves in fore and aft directions with respect to said pivot." *Id.,* col. 6, lines 17-36, Supplemental App. 8 (diagram numbers omitted).

We agree with the District Court that the claim discloses "a position-adjustable pedal assembly with an electronic pedal position sensor attached to the support member of the pedal assembly. Attaching the sensor to the support member allows the sensor to remain in a fixed position while the driver adjusts the pedal." 298 F.Supp.2d, at 586-587.

Before issuing the Engelgau patent the U.S. Patent and Trademark Office (PTO) rejected one of the patent claims that was similar to, but broader than, the present claim 4. The claim did not include the requirement that the sensor be placed on a fixed pivot point. The PTO concluded the claim was an obvious combination of the prior art disclosed in Redding and Smith, explaining:

> " 'Since the prior ar[t] references are from the field of endeavor, the purpose disclosed ... would have been recognized in the pertinent art of Redding. Therefore it would have been obvious ... to provide the device of Redding with the ... means attached to a support member as taught by Smith.' " *Id.,* at 595.

In other words Redding provided an example of an adjustable pedal and Smith explained how to mount a sensor on a pedal's support structure, and the rejected patent claim merely put these two teachings together.

Although the broader claim was rejected, claim 4 was later allowed because it included the limitation of a fixed pivot point, which distinguished the design from Redding's. *Ibid.* Engelgau had not included Asano among the prior art references, and Asano was not mentioned in the patent's prosecution. Thus, the PTO did not have before it an adjustable pedal with a fixed pivot point. The patent issued on May 29, 2001 and was assigned to Teleflex.

Upon learning of KSR's design for GM, Teleflex sent a warning letter informing KSR that its proposal would violate the Engelgau patent. " 'Teleflex believes that any supplier of a product that combines an adjustable pedal with an electronic throttle control necessarily employs technology covered by one or more' " of Teleflex's patents. *Id.,* at 585. KSR refused to enter a royalty arrangement with Teleflex; so Teleflex sued for infringement, asserting KSR's pedal infringed the Engelgau patent and two other patents. *Ibid.* Teleflex later abandoned its claims regarding the other patents and dedicated the patents to the public. The remaining contention was that KSR's pedal system for GM infringed claim 4 of the Engelgau patent. Teleflex has not argued that the other three claims of the patent are infringed by KSR's pedal, nor has Teleflex argued that the mechanical adjustable pedal designed by KSR for Ford infringed any of its patents.

C

The District Court granted summary judgment in KSR's favor. After reviewing the pertinent history of pedal design, the scope of the Engelgau patent, and the relevant prior art, the court considered the validity of the contested claim. By direction of 35 U.S.C. § 282, an issued patent is presumed valid. The District Court applied *Graham's* framework to determine whether under summary-judgment standards KSR had overcome the presumption and demonstrated that claim 4 was obvious in light of the prior art in existence when ***1738** the claimed subject matter was invented. See § 102(a).

The District Court determined, in light of the expert testimony and the parties' stipulations, that the level of ordinary skill in pedal design was " 'an undergraduate degree in mechanical engineering (or an equivalent amount of industry experience) [and] familiarity with pedal control systems for vehicles.' " 298 F.Supp.2d, at 590. The court then set forth the relevant prior art, including the patents and pedal designs described above.

Following *Graham's* direction, the court compared the teachings of the prior art to the claims of Engelgau. It found "little difference." 298 F.Supp.2d, at 590. Asano taught everything contained in claim 4 except the use of a sensor to detect the pedal's position and transmit it to the computer controlling the throttle. That additional aspect was revealed in sources such as the '068 patent and the sensors used by Chevrolet.

Under the controlling cases from the Court of Appeals for the Federal Circuit, however, the District Court was not permitted to stop there. The court was required also to apply the TSM test. The District Court held KSR had satisfied the test. It reasoned (1) the state of the industry would lead inevitably to combinations of electronic sensors and adjustable pedals, (2) Rixon provided the basis for these developments, and (3) Smith taught a solution to the wire chafing problems in Rixon, namely locating the sensor on the fixed structure of the pedal. This could lead to the combination of Asano, or a pedal like it, with a pedal position sensor.

The conclusion that the Engelgau design was obvious was supported, in the District Court's view, by the PTO's rejection of the broader version of claim 4. Had Engelgau included Asano in his patent application, it reasoned, the PTO would have found claim 4 to be an obvious combination of Asano and Smith, as it had found the broader version an obvious combination of Redding and Smith. As a final matter, the District Court held that the secondary factor of Teleflex's commercial success with pedals based on Engelgau's design did not alter its conclusion. The District Court granted summary judgment for KSR.

With principal reliance on the TSM test, the Court of Appeals reversed. It ruled the District Court had not been strict enough in applying the test, having failed to make " 'finding[s] as to the specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of [the] invention'... to attach an electronic control to the support bracket of the As-

ano assembly." 119 Fed.Appx., at 288 (brackets in original) (quoting *In re Kotzab,* 217 F.3d 1365, 1371 (C.A.Fed.2000)). The Court of Appeals held that the District Court was incorrect that the nature of the problem to be solved satisfied this requirement because unless the "prior art references address[ed] the precise problem that the patentee was trying to solve," the problem would not motivate an inventor to look at those references. 119 Fed.Appx., at 288.

Here, the Court of Appeals found, the Asano pedal was designed to solve the " 'constant ratio problem' "-that is, to ensure that the force required to depress the pedal is the same no matter how the pedal is adjusted-whereas Engelgau sought to provide a simpler, smaller, cheaper adjustable electronic pedal. *Ibid.* As for Rixon, the court explained, that pedal suffered from the problem of wire chafing but was not designed to solve it. In the court's view Rixon did not teach anything helpful to Engelgau's purpose. Smith, in turn, did not relate to adjustable pedals and did not "necessarily go to the issue of motivation ***1739** to attach the electronic control on the support bracket of the pedal assembly." *Ibid.* When the patents were interpreted in this way, the Court of Appeals held, they would not have led a person of ordinary skill to put a sensor on the sort of pedal described in Asano.

That it might have been obvious to try the combination of Asano and a sensor was likewise irrelevant, in the court's view, because " ' "[o]bvious to try" has long been held not to constitute obviousness.' " *Id.,* at 289 (quoting *In re Deuel,* 51 F.3d 1552, 1559 (C.A.Fed.1995)).

The Court of Appeals also faulted the District Court's consideration of the PTO's rejection of the broader version of claim 4. The District Court's role, the Court of Appeals explained, was not to speculate regarding what the PTO might have done had the Engelgau patent mentioned Asano. Rather, the court held, the District Court was obliged first to presume that the issued patent was valid and then to render its own independent judgment of obviousness based on a review of the prior art. The fact that the PTO had rejected the broader version of claim 4, the Court of Appeals said, had no place in that analysis.

The Court of Appeals further held that genuine issues of material fact precluded summary judgment. Teleflex had proffered statements from one expert that claim 4 " 'was a simple, elegant, and novel combination of features,' " 119 Fed.Appx., at 290, compared to Rixon, and from another expert that claim 4 was nonobvious because, unlike in Rixon, the sensor was mounted on the support bracket rather than the pedal itself. This evidence, the court concluded, sufficed to require a trial.

II

A

We begin by rejecting the rigid approach of the Court of Appeals. Throughout this Court's engagement with the question of obviousness, our cases have set forth an expansive and flexible approach inconsistent with the way the Court of Appeals applied its TSM test here. To be sure, *Graham* recognized the need for "uniformity and definiteness." 383 U.S., at 18, 86 S.Ct. 684. Yet the principles laid down in *Graham* reaffirmed the "functional approach" of *Hotchkiss,* 11 How. 248, 13 L.Ed. 683. See 383 U.S., at 12, 86 S.Ct. 684. To this end, *Graham* set forth a broad inquiry and invited courts, where appropriate, to look at any secondary considerations that would prove instructive. *Id.,* at 17, 86 S.Ct. 684.

Neither the enactment of § 103 nor the analysis in *Graham* disturbed this Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art. For over a half century, the Court has held that a "patent for a combination which only unites old elements with no change in their respective functions ... obviously withdraws what is

already known into the field of its monopoly and diminishes the resources available to skillful men." *Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp.,* 340 U.S. 147, 152, 71 S.Ct. 127, 95 L.Ed. 162 (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. Three cases decided after *Graham* illustrate the application of this doctrine.

In *United States v. Adams,* 383 U.S. 39, 40, 86 S.Ct. 708, 15 L.Ed.2d 572 (1966), a companion case to *Graham,* the Court considered the obviousness of a "wet battery" that varied from prior designs in two ways: ***1740** It contained water, rather than the acids conventionally employed in storage batteries; and its electrodes were magnesium and cuprous chloride, rather than zinc and silver chloride. The Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result. 383 U.S., at 50-51, 86 S.Ct. 708. It nevertheless rejected the Government's claim that Adams's battery was obvious. The Court relied upon the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious. *Id.,* at 51-52, 86 S.Ct. 708. When Adams designed his battery, the prior art warned that risks were involved in using the types of electrodes he employed. The fact that the elements worked together in an unexpected and fruitful manner supported the conclusion that Adams's design was not obvious to those skilled in the art.

In *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.,* 396 U.S. 57, 90 S.Ct. 305, 24 L.Ed.2d 258 (1969), the Court elaborated on this approach. The subject matter of the patent before the Court was a device combining two pre-existing elements: a radiant-heat burner and a paving machine. The device, the Court concluded, did not create some new synergy: The radiant-heat burner functioned just as a burner was expected to function; and the paving machine did the same. The two in combination did no more than they would in separate, sequential operation. *Id.,* at 60-62, 90 S.Ct. 305. In those circumstances, "while the combination of old elements performed a useful function, it added nothing to the nature and quality of the radiant-heat burner already patented," and the patent failed under § 103. *Id.,* at 62, 90 S.Ct. 305 (footnote omitted).

Finally, in *Sakraida v. Ag Pro, Inc.,* 425 U.S. 273, 96 S.Ct. 1532, 47 L.Ed.2d 784 (1976), the Court derived from the precedents the conclusion that when a patent "simply arranges old elements with each performing the same function it had been known to perform" and yields no more than one would expect from such an arrangement, the combination is obvious. *Id.,* at 282, 96 S.Ct. 1532.

[1] The principles underlying these cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative-a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

Following these principles may be more difficult in other cases than it is here because the claimed subject matter may involve more than the simple substitution of one known element for another or the

mere application of a known technique to a piece of prior art ready for the improvement. Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ***1741** ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit. See *In re Kahn,* 441 F.3d 977, 988 (C.A.Fed.2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness"). As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

B

[2] When it first established the requirement of demonstrating a teaching, suggestion, or motivation to combine known elements in order to show that the combination is obvious, the Court of Customs and Patent Appeals captured a helpful insight. See *Application of Bergel,* 48 C.C.P.A. 1102, 292 F.2d 955, 956-957 (1961). As is clear from cases such as *Adams,* a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Helpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents. The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way. In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.

In the years since the Court of Customs and Patent Appeals set forth the essence of the TSM test, the Court of Appeals no doubt has applied the test in accord with these principles in many cases. There is no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis. But when a court transforms the general principle into a rigid rule that limits the obviousness inquiry, as the Court of Appeals did here, it errs.

C

[3][4] The flaws in the analysis of the Court of Appeals relate for the most part to the court's narrow conception of the obviousness inquiry reflected in its application of the TSM test. In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the ***1742** patentee controls. What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid

under § 103. One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims.

[5] The first error of the Court of Appeals in this case was to foreclose this reasoning by holding that courts and patent examiners should look only to the problem the patentee was trying to solve. 119 Fed.Appx., at 288. The Court of Appeals failed to recognize that the problem motivating the patentee may be only one of many addressed by the patent's subject matter. The question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art. Under the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.

The second error of the Court of Appeals lay in its assumption that a person of ordinary skill attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem. *Ibid.* The primary purpose of Asano was solving the constant ratio problem; so, the court concluded, an inventor considering how to put a sensor on an adjustable pedal would have no reason to consider putting it on the Asano pedal. *Ibid.* Common sense teaches, however, that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle. Regardless of Asano's primary purpose, the design provided an obvious example of an adjustable pedal with a fixed pivot point; and the prior art was replete with patents indicating that a fixed pivot point was an ideal mount for a sensor. The idea that a designer hoping to make an adjustable electronic pedal would ignore Asano because Asano was designed to solve the constant ratio problem makes little sense. A person of ordinary skill is also a person of ordinary creativity, not an automaton.

[6] The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." *Id.,* at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

The Court of Appeals, finally, drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning. See *Graham,* 383 U.S., at 36, 86 S.Ct. 684 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to " 'guard against slipping into the use of hindsight' " (quoting *Monroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.,* 332 F.2d 406, 412 (C.A.6 1964))). Rigid preventative rules that deny factfinders recourse to common sense, however, are ***1743** neither necessary under our case law nor consistent with it.

We note the Court of Appeals has since elaborated a broader conception of the TSM test than was applied in the instant matter. See, *e.g., DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.,* 464 F.3d 1356, 1367 (2006) ("Our suggestion test is in actuality quite flexible and not only permits, but *requires,* consideration of common knowledge and common sense"); *Alza Corp. v. Mylan Labs., Inc.,* 464 F.3d 1286, 1291 (2006) ("There is flexibility in our obviousness jurisprudence because a motivation may be found *implicitly*

in the prior art. We do not have a rigid test that requires an actual teaching to combine ..."). Those decisions, of course, are not now before us and do not correct the errors of law made by the Court of Appeals in this case. The extent to which they may describe an analysis more consistent with our earlier precedents and our decision here is a matter for the Court of Appeals to consider in its future cases. What we hold is that the fundamental misunderstandings identified above led the Court of Appeals in this case to apply a test inconsistent with our patent law decisions.

III

[7] When we apply the standards we have explained to the instant facts, claim 4 must be found obvious. We agree with and adopt the District Court's recitation of the relevant prior art and its determination of the level of ordinary skill in the field. As did the District Court, we see little difference between the teachings of Asano and Smith and the adjustable electronic pedal disclosed in claim 4 of the Engelgau patent. A person having ordinary skill in the art could have combined Asano with a pedal position sensor in a fashion encompassed by claim 4, and would have seen the benefits of doing so.

A

Teleflex argues in passing that the Asano pedal cannot be combined with a sensor in the manner described by claim 4 because of the design of Asano's pivot mechanisms. See Brief for Respondents 48-49, and n. 17. Therefore, Teleflex reasons, even if adding a sensor to Asano was obvious, that does not establish that claim 4 encompasses obvious subject matter. This argument was not, however, raised before the District Court. There Teleflex was content to assert only that the problem motivating the invention claimed by the Engelgau patent would not lead to the solution of combining of Asano with a sensor. See Teleflex's Response to KSR's Motion for Summary Judgment of Invalidity in No. 02-74586 (ED Mich.), pp. 18-20, App. 144a-146a. It is also unclear whether the current argument was raised before the Court of Appeals, where Teleflex advanced the nonspecific, conclusory contention that combining Asano with a sensor would not satisfy the limitations of claim 4. See Brief for Plaintiffs-Appellants in No. 04-1152 (CA Fed.), pp. 42-44. Teleflex's own expert declarations, moreover, do not support the point Teleflex now raises. See Declaration of Clark J. Radcliffe, Ph.D., Supplemental App. 204-207; Declaration of Timothy L. Andresen, *id.*, at 208-210. The only statement in either declaration that might bear on the argument is found in the Radcliffe declaration:

> "Asano ... and Rixon ... are complex mechanical linkage-based devices that are expensive to produce and assemble and difficult to package. It is exactly these difficulties with prior art designs that [Engelgau] resolves. The use of an adjustable pedal with a single pivot reflecting pedal position combined with an electronic control mounted between the ***1744** support and the adjustment assembly at that pivot was a simple, elegant, and novel combination of features in the Engelgau '565 patent." *Id.*, at 206, ¶ 16.

Read in the context of the declaration as a whole this is best interpreted to mean that Asano could not be used to solve "[t]he problem addressed by Engelgau '565[:] to provide a less expensive, more quickly assembled, and smaller package adjustable pedal assembly with electronic control." *Id.*, at 205, ¶ 10.

The District Court found that combining Asano with a pivot-mounted pedal position sensor fell within the scope of claim 4. 298 F.Supp.2d, at 592-593. Given the sigificance of that finding to the District Court's judgment, it is apparent that Teleflex would have made clearer challenges to it if it intended to preserve this claim. In light of Teleflex's failure to raise the argument in a clear fashion, and the silence of the Court of Appeals on the issue, we take the District Court's conclusion on the point to be correct.

B

The District Court was correct to conclude that, as of the time Engelgau designed the subject matter in claim 4, it was obvious to a person of ordinary skill to combine Asano with a pivot-mounted pedal position sensor. There then existed a marketplace that created a strong incentive to convert mechanical pedals to electronic pedals, and the prior art taught a number of methods for achieving this advance. The Court of Appeals considered the issue too narrowly by, in effect, asking whether a pedal designer writing on a blank slate would have chosen both Asano and a modular sensor similar to the ones used in the Chevrolet truckline and disclosed in the '068 patent. The District Court employed this narrow inquiry as well, though it reached the correct result nevertheless. The proper question to have asked was whether a pedal designer of ordinary skill, facing the wide range of needs created by developments in the field of endeavor, would have seen a benefit to upgrading Asano with a sensor.

In automotive design, as in many other fields, the interaction of multiple components means that changing one component often requires the others to be modified as well. Technological developments made it clear that engines using computer-controlled throttles would become standard. As a result, designers might have decided to design new pedals from scratch; but they also would have had reason to make pre-existing pedals work with the new engines. Indeed, upgrading its own pre-existing model led KSR to design the pedal now accused of infringing the Engelgau patent.

For a designer starting with Asano, the question was where to attach the sensor. The consequent legal question, then, is whether a pedal designer of ordinary skill starting with Asano would have found it obvious to put the sensor on a fixed pivot point. The prior art discussed above leads us to the conclusion that attaching the sensor where both KSR and Engelgau put it would have been obvious to a person of ordinary skill.

The '936 patent taught the utility of putting the sensor on the pedal device, not in the engine. Smith, in turn, explained to put the sensor not on the pedal's footpad but instead on its support structure. And from the known wire-chafing problems of Rixon, and Smith's teaching that "the pedal assemblies must not precipitate any motion in the connecting wires," Smith, col. 1, lines 35-37, Supplemental App. 274, the designer would know to place the sensor on a nonmoving part of the pedal structure. The most obvious nonmoving point on the structure from which a sensor can ***1745** easily detect the pedal's position is a pivot point. The designer, accordingly, would follow Smith in mounting the sensor on a pivot, thereby designing an adjustable electronic pedal covered by claim 4.

Just as it was possible to begin with the objective to upgrade Asano to work with a computer-controlled throttle, so too was it possible to take an adjustable electronic pedal like Rixon and seek an improvement that would avoid the wire-chafing problem. Following similar steps to those just explained, a designer would learn from Smith to avoid sensor movement and would come, thereby, to Asano because Asano disclosed an adjustable pedal with a fixed pivot.

Teleflex indirectly argues that the prior art taught away from attaching a sensor to Asano because Asano in its view is bulky, complex, and expensive. The only evidence Teleflex marshals in support of this argument, however, is the Radcliffe declaration, which merely indicates that Asano would not have solved Engelgau's goal of making a small, simple, and inexpensive pedal. What the declaration does not indicate is that Asano was somehow so flawed that there was no reason to upgrade it, or pedals like it, to be compatible with modern engines. Indeed, Teleflex's own declarations refute this conclusion. Dr. Radcliffe states that Rixon suffered from the same bulk and complexity as did Asano. See *id.*, at 206. Teleflex's other expert, however, explained that Rixon was itself designed by adding a sensor to a pre-existing mechanical

pedal. See *id.,* at 209. If Rixon's base pedal was not too flawed to upgrade, then Dr. Radcliffe's declaration does not show Asano was either. Teleflex may have made a plausible argument that Asano is inefficient as compared to Engelgau's preferred embodiment, but to judge Asano against Engelgau would be to engage in the very hindsight bias Teleflex rightly urges must be avoided. Accordingly, Teleflex has not shown anything in the prior art that taught away from the use of Asano.

Like the District Court, finally, we conclude Teleflex has shown no secondary factors to dislodge the determination that claim 4 is obvious. Proper application of *Graham* and our other precedents to these facts therefore leads to the conclusion that claim 4 encompassed obvious subject matter. As a result, the claim fails to meet the requirement of § 103.

We need not reach the question whether the failure to disclose Asano during the prosecution of Engelgau voids the presumption of validity given to issued patents, for claim 4 is obvious despite the presumption. We nevertheless think it appropriate to note that the rationale underlying the presumption-that the PTO, in its expertise, has approved the claim-seems much diminished here.

IV

[8] A separate ground the Court of Appeals gave for reversing the order for summary judgment was the existence of a dispute over an issue of material fact. We disagree with the Court of Appeals on this point as well. To the extent the court understood the *Graham* approach to exclude the possibility of summary judgment when an expert provides a conclusory affidavit addressing the question of obviousness, it misunderstood the role expert testimony plays in the analysis. In considering summary judgment on that question the district court can and should take into account expert testimony, which may resolve or keep open certain questions of fact. That is not the end of the issue, however. The ultimate judgment of obviousness is a legal determination. *Graham,* 383 U.S., at 17, 86 S.Ct. 684. Where, as here, the content of the prior art, the scope of the patent ***1746** claim, and the level of ordinary skill in the art are not in material dispute, and the obviousness of the claim is apparent in light of these factors, summary judgment is appropriate. Nothing in the declarations proffered by Teleflex prevented the District Court from reaching the careful conclusions underlying its order for summary judgment in this case.

* * *

We build and create by bringing to the tangible and palpable reality around us new works based on instinct, simple logic, ordinary inferences, extraordinary ideas, and sometimes even genius. These advances, once part of our shared knowledge, define a new threshold from which innovation starts once more. And as progress beginning from higher levels of achievement is expected in the normal course, the results of ordinary innovation are not the subject of exclusive rights under the patent laws. Were it otherwise patents might stifle, rather than promote, the progress of useful arts. See U.S. Const., Art. I, § 8, cl. 8. These premises led to the bar on patents claiming obvious subject matter established in *Hotchkiss* and codified in § 103. Application of the bar must not be confined within a test or formulation too constrained to serve its purpose.

KSR provided convincing evidence that mounting a modular sensor on a fixed pivot point of the Asano pedal was a design step well within the grasp of a person of ordinary skill in the relevant art. Its arguments, and the record, demonstrate that claim 4 of the Engelgau patent is obvious. In rejecting the District Court's rulings, the Court of Appeals analyzed the issue in a narrow, rigid manner inconsistent with § 103 and our precedents. The judgment of the Court of Appeals is reversed, and the case remanded for further proceedings consistent with this opinion.

It is so ordered.

U.S.,2007.
KSR Intern. Co. v. Teleflex Inc.
127 S.Ct. 1727, 167 L.Ed.2d 705, 75 USLW 4289,
82 U.S.P.Q.2d 1385, 07 Cal. Daily Op. Serv. 4654,
20 Fla. L. Weekly Fed. S 248

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520 F.3d 1358
520 F.3d 1358, 86 U.S.P.Q.2d 1196

▷

United States Court of Appeals,Federal Circuit.
ORTHO-McNEIL PHARMACEUTICAL, INC., Plaintiff-Appellee,
v.
MYLAN LABORATORIES, INC., and Mylan Pharmaceuticals, Inc., Defendants-Appellants.
No. 2007-1223.

March 31, 2008.

Background: Patentee brought action against competitor alleging infringement of patent relating to chemical formula of anticonvulsive drug topiramate. The United States District Court for the District of New Jersey, Stanley R. Chesler, J., denied competitor's motion for summary judgment, 2005 WL 1683644, granted patentee's motions for partial summary judgment, 2006 WL 1517749, 2006 WL 2865469, 2007 WL 432792, and granted patentee's motion for entry of final judgment, 2007 WL 869545.Competitor appealed.

Holdings: The Court of Appeals, Rader, Circuit Judge, held that:
(1) term "and," in claim of patent, was used to connote alternatives rather than in the additive sense;
(2) patentee's statements about prior art references for chemical compounds made during patent prosecution were not misrepresentations;
(3) patent claims were not obvious; and
(4) patent specification disclosing that the average adult requires 30-2000 milligrams of claimed compounds administered in two to four doses at 10-500 milligrams adequately enabled claims of patent.

Affirmed.

West Headnotes

[1] Patents 291 ⇐101(2)

291 Patents
291IV Applications and Proceedings Thereon
291k101 Claims
291k101(2) k. Construction in General. Most Cited Cases
Term "and," in claim of patent relating to chemical formula of anticonvulsive drug topiramate, was used to connote alternatives rather than in the additive sense; "and" appeared in conjunction with adverbs "independently" and "together," and construing the claim to require a conjunctive meaning of "and" would have rendered several dependent claims meaningless.

[2] Patents 291 ⇐165(3)

291 Patents
291IX Construction and Operation of Letters Patent
291IX(B) Limitation of Claims
291k165 Operation and Effect of Claims in General
291k165(3) k. Construction of Language of Claims in General. Most Cited Cases
A nonsensical result does not require the court to redraft the claims of a patent.

[3] Patents 291 ⇐97

291 Patents
291IV Applications and Proceedings Thereon
291k97 k. Patent Office and Proceedings Therein in General. Most Cited Cases
Patentee's statements about prior art references for chemical compounds made during patent prosecution of patent relating to anticonvulsive drug topiramate were not misrepresentations, despite argument that patentee's statements were inconsistent with its own information about the compounds; statements merely accurately characterized references as claiming limited utility for compounds, and made no assertions about the compounds themselves.

[4] Patents 291 ⇐16.25

291 Patents

291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical Compounds. Most Cited Cases
Claims for patent relating to anticonvulsive drug topiramate were not obvious; challenges of inventive process would have prevented one of ordinary skill in the art from traversing the multiple obstacles to easily produce the invention in light of the evidence available at the time of invention.

[5] Patents 291 ⚿99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases
Specification of patent relating to chemical formula of anticonvulsive drug topiramate, disclosing that the average adult requires 30-2000 milligrams of the claimed compounds administered in two to four doses at 10-500 milligrams, adequately enabled claims of patent, despite argument that anticonvulsive effective amount was unclear and its determination would require undue experimentation.

[6] Patents 291 ⚿99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases
A patent specification that enables an invention will teach those ordinarily skilled in the art to make and use the full scope of the claimed invention without undue experimentation.

[7] Health 198H ⚿319

198H Health
198HI Regulation in General
198HI(E) Drugs; Medical Devices and Instruments
198Hk315 Applications and Approvals
198Hk319 k. Generic and Orphan Drugs; Market Exclusivity. Most Cited Cases
Statute relating to Food and Drug Administration's (FDA) responsibilities in approving an abbreviated new drug application (ANDA) after finding a patent infringed does not limit a court's authority to reset the effective date of an ANDA for conditions other than those listed. Federal Food, Drug, and Cosmetic Act, § 505, 21 U.S.C.A. § 355; 35 U.S.C.A. § 271.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases
4,513,006. Infringed.

***1360** Harry J. Roper, Jenner & Block LLP, of Chicago, Illinois, argued for plaintiff-appellee. With him on the brief were Aaron A. Barlow and Eric L. Lohrenz, of Chicago, Illinois, and Marc A. Goldman, of Washington, DC.
David J. Harth, Heller Ehrman LLP, of Madison, Wisconsin, argued for defendants-appellants. With him on the brief were Randy J. Kozel, of Madison, Wisconsin, and Shannon M. Bloodworth, of Washington, DC.

Before MICHEL, Chief Judge, RADER and LINN, Circuit Judges.

RADER, Circuit Judge.
The United States District Court for the District of New Jersey permanently enjoined Mylan Laboratories, Inc. from infringing Ortho-McNeil Pharmaceutical Inc.'s U.S. Patent No. 4,513,006 ('006). The '006 patent claims the anticonvulsive drug topiramate. The trial court also reset the effective approval date for Mylan's Abbreviated New Drug Application (ANDA). Because the district court correctly ruled on claim construction, inequitable conduct, obviousness, and enablement, and because the district court did not err in resetting the effective date of Mylan's ANDA under 35 U.S.C. §

271(e)(4)(A), this court affirms.

I

Topiramate (marketed by Ortho-McNeil as TOPOMAX®) is a significant epilepsy drug with sales exceeding $1 billion annually. Ortho-McNeil scientist Dr. Bruce Maryanoff invented this pharmaceutical during a search for new antidiabetic drugs. Topiramate is a reaction intermediate in the synthesis Dr. Maryanoff ran as part of his antidiabetic efforts. Unexpectedly, Dr. Maryanoff discovered that this particular intermediate had powerful anticonvulsant properties. After extensive testing, clinical trials, and substantial investment, Ortho-McNeil showed that the compound was safe and effective leading to FDA approval.

This cause of action arose under the Hatch-Waxman Act. 21 U.S.C. § 355. Under that Act, Mylan filed an ANDA with the FDA with a paragraph IV certification asserting that Ortho-McNeil's '006 patent is invalid or not infringed. Within 45 days, Ortho-McNeil filed an infringement suit under 35 U.S.C. § 271(e)(2) against Mylan thus triggering the 30-month stay on approval of Mylan's ANDA.

After a Markman proceeding to set the meaning of the claim terms, the district court rejected Mylan's position that claim 1 of the '006 patent does not cover topiramate. Indeed, in light of the district court's claim construction ruling, Mylan stipulated that its generic topiramate infringes claims 1, 2, 4, 5, 6, 7, 8, 11 and 12 of the '006 patent. On summary judgment, the trial court also ruled against Mylan's affirmative defenses of unenforceability due to inequitable conduct and invalidity based on obviousness and non-enablement. After entry of final judgment, Mylan now appeals the district court's claim construction as well as the dismissal of its affirmative defenses of inequitable conduct, obviousness, and non-enablement.

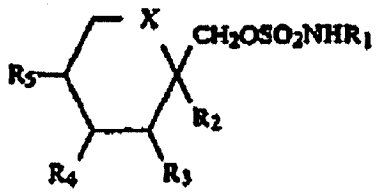
II

This court reviews a grant of summary judgment without deference. *Johns Hopkins Univ. v. CellPro, Inc.,* 152 F.3d 1342, 1353 (Fed.Cir.1998). This court must decide for itself "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed.R.Civ.P. 56(c); *Celotex Corp. v. Catrett,* 477 U.S. 317, 322, 106 S.Ct. 2548, 91 L.Ed.2d 265 (1986). In deciding these ***1361** questions, this court draws all justifiable inferences in the nonmovant's favor. *Anderson v. Liberty Lobby, Inc.,* 477 U.S. 242, 255, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986). This court also reviews claim construction as a matter of law without deference. *Cybor Corp. v. FAS Techs., Inc.,* 138 F.3d 1448, 1456 (Fed.Cir.1998) (en banc).

[1] Mylan argues that the district court improperly construed the word *and* to mean *or* in independent claim 1, and under the proper construction, the claim does not cover topiramate. In light of the plain language of independent claim 1, several dependent claims, the specification, and the extrinsic evidence, this court sustains the trial court's ruling that, in the circumstances of this case, claim 1's use of the term *and* means *or*.

Claim 1 of the '006 patent states:

1. A sulfamate of the following formula (I):

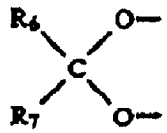


wherein

X is oxygen;

R1 is hydrogen or alkyl; and

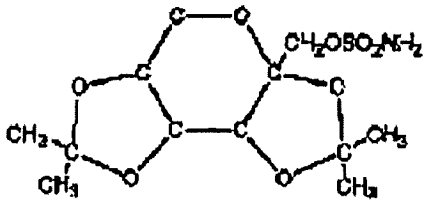
R2, R3, R4 and R5 are independently hydrogen or lower alkyl and R2 and R3 and/or R4 and R5 together may be a group of the following formula (II):



wherein

R6 and R7 are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

Topiramate has the following structure:



In the molecule topiramate, R2 and R3 and R4 and R5 together are a group of formula (II), wherein R6 and R7 are methyl. Mylan argues that the use of the term *and* precludes the claim from encompassing topiramate. In context, the term *and* falls between several R group recitations:

> R2, R3, R4, and R5 are independently hydrogen or lower alkyl *and* R2 and R3 and/or R4 and R5 together may be a group of formula (II) (emphasis added).

On this basis, Mylan argues that the phrase quoted above contains two independent claim limitations: (1) that "R2, R3, R4, and R5 are independently hydrogen or lower alkyl"*and* (2) that "R2 and R3 and/or R4 and R5 together may be a group of formula (II)." Under Mylan's construction, both of these limitations must be met in order for a compound to infringe. Both of these limitations are not met in topiramate. None of the R2, R3, R4, and R5 subunits are hydrogen or lower alkyl because both R2 and R3 and R4 and R5 together are a group of formula (II).

To the contrary, the claim language depicts two subsets of compounds, but does not require their simultaneous existence. In one subset of compounds covered by claim 1, the groups R2, R3, R4,

and R5 are independent of one another, in which case, according to the claim, they are either hydrogen or lower alkyl. In a second subset of compounds covered by claim 1, ***1362** the R2 through R5 groups are not independent, but rather R2 and R3 are together, and/or R4 and R5 are together, to form either one or two groups of formula (II). Topiramate is an example of this type of compound. In it, R2 and R3 are arranged together in a group, as are R4 and R5. Thus, as used in this claim, *and* conjoins mutually exclusive possibilit- ies.

The claim also does not use *and* in isolation but in a larger context that clarifies its meaning. Specifically, *and* appears in conjunction with the adverbs *independently* and *together.* As the district court explained, these terms signal that *and* links alternatives that occur under the different conditions of independence or togetherness. In context, it is clear that one of the subunits (R2, R3, R4, or R5) does not always have to be either a hydrogen or lower alkyl.

The larger context of this patent also supports this claim meaning. Construing claim 1 to require a conjunctive meaning of *and* would render several dependent claims meaningless. Claims 2, 5, 9, and 10 would cover nothing if the *and* at issue must be conjunctive. This court has explained: "Other claims of the patent in question ... can also be valuable sources of enlightenment as to the meaning of a claim term." *Phillips v. AWH Corp.,* 415 F.3d 1303, 1314 (Fed.Cir.2005) (en banc) (citing *Vitronics Corp. v. Conceptronic Inc.,* 90 F.3d 1576, 1582 (Fed.Cir.2003)). Thus, this court strives to reach a claim construction that does not render claim language in dependent claims meaningless. *Rambus Inc. v. Infineon Tech. AG,* 318 F.3d 1081, 1093 (Fed.Cir.2003).

The specification also supports the district court's reading of *and.* The specification thus uses the word *and* to link alternative chemical structures. In column 1 lines 47-50 the specification provides:

> R2, R3, R4 and R5 are independently hydrogen or lower alkyl *and,* when X is CH2, R4 and R5 may be alkene groups joined to form a benzene ring *and* when X is oxygen, R2 and R3 and/or R4 and R5 together may be a methylenedioxy group of the following formula II....

(emphases added). Without question, this passage within the specification shows use of the word *and* to join alternatives.

While extrinsic evidence "can shed useful light on the relevant art," this court considers such evidence "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.' " *Phillips,* 415 F.3d at 1317 (citations omitted). Because the plain language of claim 1, the dependent claims, and the specification support the district court's reading, this court does not need to consult extrinsic evidence. Nonetheless, this court notes that dictionary definitions of *and,* while most often listing the additive sense as the most common usage of the term, also show usage of the term to connote alternatives. *Webster's Third New International Dictionary* (2002). In the circumstances of this case, the use of *and* to express alternatives was chosen and adequately expressed by the applicant. Thus, extrinsic evidence too offers support for the district court's reading of the disputed term.

[2] In *Chef America Inc. v. Lamb Weston, Inc.,* this court explained that a patent must be interpreted "as written, not as the patentees wish they had written it." 358 F.3d 1371, 1374 (Fed.Cir.2004). In other words, courts may not redraft claims, whether to make them operable or to sustain their validity. *Id.* Even "a nonsensical result does not require the court to redraft the claims of the ... patent." *Id.* (citing *Process Control Corp. v. HydReclaim Corp.,* 190 F.3d 1350, 1357 (Fed.Cir.1999)). However, *Chef America* does not require this court or the district court to interpret *and* according to its most common***1363** usage in the dictionary. To the contrary, this court and the district court must interpret the term to give proper meaning to the claim in light of the language and intrinsic evidence. Giving

and its most common dictionary meaning would produce in this case the nonsensical result of not covering topiramate and rendering several other dependent claims meaningless. In *Chef America,* the only possible interpretation of the claim led to a nonsensical result. This situation is distinguishable because claim 1 can and should be interpreted as the patentees intended, with the meaning of *and* connoting alternatives.

In sum, the district court properly interpreted the claim. This court detects no error in its claim construction.

III

[3] Mylan accuses Ortho-McNeil of committing inequitable conduct by failing to disclose the results of non-public tests it conducted on the prior art Kochetkov compounds to the Patent Office. In fact, the applicant submitted the Kochetkov references themselves, but not results from the tests that Dr. Maryanoff conducted on the compounds. Mylan says that Ortho-McNeil's statements about the Kochetkov references during prosecution were inconsistent with Ortho-McNeil's own information that the compounds had anticonvulsant properties. During prosecution, Ortho-McNeil said the following:

> It should be noted that the utility disclosed in the Kochetkov references AR-AU is extremely limited and narrow. These compounds are merely taught as being convenient derivatives of monosaccharide sulfates to allow separation of such sulfates from each other with regeneration of the original sulfate thereafter. No teaching is provided for any actual utility of the sulfamates or sulfates described in AR-AU and it is respectfully submitted that there is no motivation for one skilled in the art reading AR-AU to go beyond the pyranoses disclosed therein to arrive at Applicant's invention.

Mylan claims that this was a misrepresentation because in-house test results demonstrated that the Kochetkov compounds had anticonvulsive properties. To the contrary, the district court found, and this court agrees, that Ortho-McNeil did not make misrepresentations to the Patent Office during prosecution. The quoted passage merely accurately characterizes the references as claiming limited utility for the Kochetkov compounds. Ortho-McNeil made no assertions about the compounds themselves, but only repeated the disclosures of the Kochetkov references.

The same observation applies to the sentence following the passage quoted above:

> As explained above, the pyranoses of AR-AU are entirely different in structure and use than the pyranoses of the present invention, and given the minimal usefulness of the AR-AU compounds, it would not be obvious to one skilled in the art to go beyond AR-AU to the pyranose structures of the present invention.

Again, as the opening phrase of the above quote confirms, the applicant is repeating the disclosures of the Kochetcov references, not characterizing the compounds themselves. Read in context, the Kochetkov references do not disclose any utility. On this point, the applicant is correct. Moreover, the applicant did not assert that the compounds themselves possess no utility. Thus, Ortho-McNeil made no misrepresentations to the Patent Office. Accordingly the district court correctly dismissed Mylan's affirmative defense of inequitable conduct.

IV

[4] Dr. Laurens Anderson, Mylan's expert, asserts that a person of ordinary skill ***1364** in the art faced with finding a diabetes drug (as Dr. Maryannoff was) would necessarily design an FBPase inhibitor. Mylan cites *KSR International Co. v. Teleflex Inc.,* for the proposition that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable

solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." --- U.S. ----, 127 S.Ct. 1727, 1742, 167 L.Ed.2d 705 (2007). The record, however, shows that even if an ordinarily skilled artisan sought an FBPase inhibitor, that person would not have chosen topiramate. Moreover this invention, contrary to Mylan's characterization, does not present a finite (and small in the context of the art) number of options easily traversed to show obviousness. The passage above in *KSR* posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness. In this case, the record shows that a person of ordinary skill would not even be likely to start with 2,3:4,5 di-isopropylidene fructose (DPF), as Dr. Maryanoff did. Beyond that step, however, the ordinarily skilled artisan would have to have some reason to select (among several unpredictable alternatives) the exact route that produced topiramate as an intermediate. Even beyond that, the ordinary artisan in this field would have had to (at the time of invention without any clue of potential utility of topiramate) stop at that intermediate and test it for properties far afield from the purpose for the development in the first place (epilepsy rather than diabetes). In sum, this clearly is not the easily traversed, small and finite number of alternatives that *KSR* suggested might support an inference of obviousness. *Id.* at 1742.

In other words, Mylan's expert, Dr. Anderson, simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention of topiramate was obvious. Of course, this reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "*would have been obvious at the time the invention was made.*" 35 U.S.C. § 103(a) (emphasis added). In retrospect, Dr. Maryanoff's pathway to the invention, of course, seems to follow the logical steps to produce these properties, but at the time of invention, the inventor's insights, willingness to confront and overcome obstacles, and yes, even serendipity, cannot be discounted.

Speaking before *KSR,* the district court endorsed a "rigorous application" of the teaching, suggestion, or motivation (TSM) test. In *KSR,* the Supreme Court explained that a "rigid" TSM test "is incompatible with our precedents." *KSR,* 127 S.Ct. at 1741. Mylan thus contends that the district court erred by rigorously applying the TSM test. The Supreme Court explained its reason for castigating a "rigid" TSM test: "The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." *Id.* Indeed a rigid requirement of reliance on written prior art or patent references would, as the Supreme Court noted, unduly confine the use of the knowledge and creativity within the grasp of an ordinarily skilled artisan. *Id.* at 1742.

As this court has explained, however, a flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis such as occurred in this case. *In re Translogic Tech., Inc.,* 504 F.3d 1249, 1257 (Fed.Cir.2007) ("[A]s the Supreme Court suggests, a flexible approach***1365** to the TSM test prevents hindsight and focuses on evidence before the time of invention."). The TSM test, flexibly applied, merely assures that the obviousness test proceeds on the basis of evidence-teachings, suggestions (a tellingly broad term), or motivations (an equally broad term)-that arise before the time of invention as the statute requires. As *KSR* requires, those teachings, suggestions, or motivations need not always be written references but may be found within the knowledge and creativity of ordinarily skilled artisans.

In this case, the record amply supports the district court's finding of nonobviousness. This court detects no rigid application of the evidentiary requirements for obviousness in the district court's analysis. As noted above, the challenges of this inventive

process would have prevented one of ordinary skill in this art from traversing the multiple obstacles to easily produce the invention in light of the evidence available at the time of invention. Of particular importance beyond the prima facie analysis, this court also detects evidence of objective criteria showing nonobviousness. Specifically, the record shows powerful unexpected results (anticonvulsive activity) for topiramate. The record also shows skepticism of experts and copying-other respected sources of objective evidence of nonobviousness-as well as commercial success. As this court has repeatedly explained, this evidence is not just a cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of nonobviousness. *Catalina Lighting, Inc. v. Lamps Plus, Inc.,* 295 F.3d 1277, 1288 (Fed.Cir.2002) ("Objective indicia may often be the most probative and cogent evidence of nonobviousness in the record.") (internal citation omitted). *See also PharmaStem Therapeutics Inc. v. Viacell, Inc.,* 491 F.3d 1342; *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.,* 471 F.3d 1369.

Mylan asserts that method of use claims 6-8 are also obvious. But if claim 1 is not obvious then claims 6-8 also cannot be obvious because they all depend from a nonobvious claim. *In re Fritch,* 972 F.2d 1260, 1266 (Fed.Cir.1992) ("[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious."). Accordingly, the method of use claims are nonobvious as well.

V

[5][6] Mylan asserts that claims 6-8 are not enabled because an *anticonvulsively effective* amount is unclear and its determination would require undue experimentation. A specification that enables an invention will teach those ordinarily skilled in the art to make and use the full scope of the claimed invention without undue experimentation. *Genentech Inc. v. Novo Nordisk of N. Am. Inc.,* 108 F.3d 1361, 1365 (Fed.Cir.1997).

The '006 specification discloses that the average adult requires 30-2000 milligrams of the claimed compounds administered in two to four doses of 10-500 milligrams. The specification also teaches a skilled artisan to use the claimed compounds in a manner similar to the drug phenytoin. Further the specification directs the reader to a reference by L.S. Goodman, which teaches that after establishment of a low initial dose, the dosage is increased at appropriate intervals as required for control of seizures or as limited by toxicity with further adjustments according to plasma drug concentrations. L.S. Goodman, et al., *The Pharmacological Basis of Therapeutics,* 201-26 (5th ed.1975). This court sustains the district court's judgment that this disclosure adequately enables claims 6-8. Further, even if clinical trials informed the anticonvulsively effective amount, this record does not show that extensive or "undue" tests would be required*1366 to practice the invention. The district court was correct in summarily dismissing Mylan's non-enablement defense.

VI

When a generic manufacturer files an ANDA with a paragraph IV certification, Hatch-Waxman grants the brand name pharmaceutical manufacturer a 30-month stay in the approval of that ANDA within which to litigate its case. 21 U.S.C. § 355(j)(5)(B)(iii). At the expiration of the 30 months, the ANDA is automatically approved unless the court grants a preliminary injunction or finds infringement. Because neither of those two events occurred before expiration of 30 months, the FDA approved Mylan's ANDA by operation of law. Therefore, after determining infringement, the district court reset the effective date of approval pursuant to 35 U.S.C. § 271(e)(4)(A), which provides:

> (4) For an act of infringement described in paragraph (2)(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of

> the expiration of the patent which has been infringed.

Although the statute does not expressly reset the effective date when the 30-month stay expires before the patent is found to be infringed or a preliminary injunction granted, the statute, as informed by its legislative history, supports the district court's action of resetting the effective date. The House Report accompanying the Hatch-Waxman Act explains: "[I]n the case where an ANDA had been approved, the order would mandate a change in the effective date." H.R.Rep. No. 98-857, at 46 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2679.

Mylan argues that the district court's order is inconsistent with 21 U.S.C. § 355(j)(5)(B)(iii), which lays out two measures for delaying an ANDA's approval:

> 21 U.S.C. § 355(j)(5)(B)(iii)(II)(bb) provides: if the district court decides that the patent has been infringed before the expiration of the 30 month period, then the FDA's approval shall be made effective on the date specified by the district court in a court order under 35 U.S.C. § 271(e)(4)(A).
>
> 21 U.S.C. § 355(j)(5)(B)(iii)(IV) provides: if before the expiration of [the 30 month stay] the court grants a preliminary judgment ... and if the court decides that such patent has been infringed then the approval shall be made effective as in subclause (II).

[7] The district court, however, did not ignore these express conditions when resetting the effective date. Considering 35 U.S.C. § 271, the district court correctly discerned that the provisions quoted above do not limit the authority of the district court to reset the effective date in circumstances similar to those statutorily listed as indeed suggested by the legislative history for the provision. Indeed 21 U.S.C. § 355 does not limit a court's authority to reset for conditions other than those listed. This provision, directed at the FDA, instructs the agency regarding its responsibilities to process an ANDA. This provision does not limit the court's authority as noted. The district court was correct to reset the effective date of an ANDA directly under 35 U.S.C. § 271 without going through 21 U.S.C. § 355.

VII

In view of all the intrinsic and extrinsic evidence, the district court correctly construed claim 1 to cover Ortho-McNeil's epilepsy drug topiramate. Accordingly, this court affirms the district court's decision to permanently enjoin Mylan from infringing the '006 patent. This court also ***1367** affirms the dismissal of Mylan's invalidity defenses based on obviousness, inequitable conduct, and non-enablement and finds no error in the district court's decision to reset the effective date of Mylan's ANDA to a date not earlier than the date of expiration of the patent.

AFFIRMED

C.A.Fed. (N.J.),2008.
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